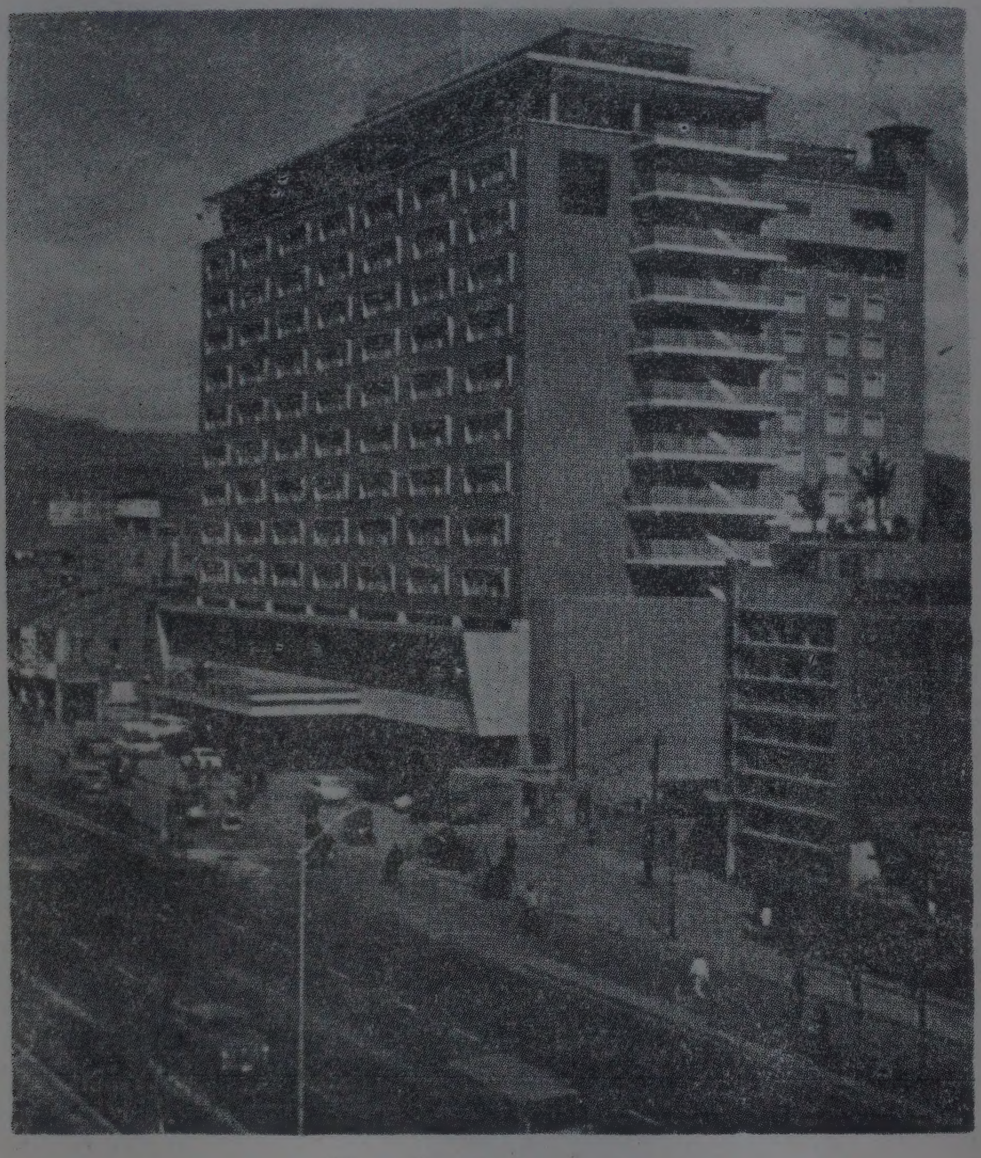
PROGRAMS

of the

VIIth Tuberculosis Conference of the Eastern Region of the International Union Against Tuberculosis

Taipei, Taiwan
Republic of China
November 16-21, 1970



The Conference is
held at
Ambassador Hotel
Taipei City

Sponsored by
The National Tuberculosis
Association of the
Republic of China

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Delegates from the member countries of the Eastern Region:

歡迎

Welcome

よくいらっしゃいました

환영합니다

ยินดีต้อนรับ

HOAN NGHÊNH

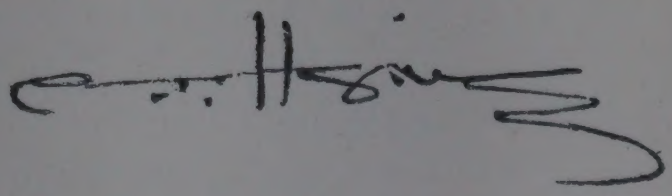
SELAMAT DATANG

Our welcome brings greetings as you come to the Republic of China to attend the VIIth Tuberculosis Conference of the Eastern Region of the International Union Against Tuberculosis.

We in the Republic of China are honored that our country has been chosen for this important Conference.

As we gather to discuss our present day knowledge and experience with tuberculosis, I am sure that the time spent in this week will be profitable to each of us.

I thank you for coming.



C. T. Hsing, M. D.
Chairman
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Officers of the Eastern Region of the International Union Against Tuberculosis

President:

Dr. J. S. Sodhy, *Malaysia*

Immediate past president:

Dr. Cotter Harvey, *Australia*

Vice-President:

Dr. M. Yamaguchi, *Japan*

Secretary/Treasurer:

Dr. N. C. Sen-Gupta, *Singapore*

Committee Members:

Mr. B. M. Cariappa, *India*
Dr. Ninart Chinchoti, *Thailand*
Dr. James Isbister, *Australia*
Dr. C. T. Hsing, *Republic of China*
Sister Mary Aquinas, *Hong Kong*
Dr. Heraldo Del Castillo, *Philippines*

Organizing Committee of the Conference

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Dr. C. T. Hsing

Members:

Dr. H. H. Meng
Dr. C. K. Wen
Miss C. M. Ho
Mr. K. T. Pai
Mr. C. F. Wu

Advicers.

Dr. C. W. Chao
Dr. S. W. Luan
Dr. C. C. Chang
Dr. T. Y. Tseng

Schedule of the 7th TB Conference

	Morning Session		Afternoon Session
15th	Executive meeting		Business meeting
16th	Opening Ceremony	Registration	Presentation of Tuberculosis Control Programs in Taiwan
17th	Chemotherapy		Chemotherapy
18th	Case-finding		Visit rural health stations
19th	BCG vaccination		Functions of voluntary organizations
20th	Field trip		Field trip
21st	Miscellaneous	Closing Remarks	

INAUGURAL SESSION

VIIth Tuberculosis Conference of the Eastern Region
of the International Union Against Tuberculosis

Ambassador Hotel, Taipei City
11 a.m., November 16, 1970

PROGRAM

Dr. J. S. Sodhy, Presiding

Address by Madame Chiang Kai-shek

Address by Director of the Health Department of the Ministry of Interior — Dr. C. K. Chang

Address by Executive Director of the International Union Against Tuberculosis — Dr. Johs. Holm

Address by Representative of the World Health Organization — Dr. T. Okuno

Conference declared open — Dr. J. S. Sodhy

SCIENTIFIC SESSION

November 16, 1970

Monday Morning

8:00–11:00 a.m. REGISTRATION

11:00–12:00 a.m. OPENING CEREMONY

Monday Afternoon

Chairman: Dr. J. S. Sodhy, *Malaysia*
Co-chairman: Dr. S. P. Yang, *Republic of China*

1:30 – 3:00 p.m.

Economic development in Taiwan

Mr. Y. S. Sun
Minister
Ministry of Economics

The development of education in Taiwan

Mr. C. C. Pan
Commissioner
Department of Education

Public health in Taiwan

Dr. T. Y. Lee
Commissioner
Department of Health

3:00 – 3:30 p.m. COFFEE BREAK

3:30 – 5:00 p.m.

Chairman: Dr. N. T. Chuc, *Vietnam*
Co-chairman: Dr. Ho Sung Song, *Republic of Korea*

Taiwan provincial tuberculosis control program	Dr. C. W. Chao
Tuberculosis control program of the educational workers	Dr. H. H. Meng
Tuberculosis control program of the retired service-men	Dr. J. P. Lu

November 17, 1970

Tuesday Morning

Chairman: Dr. M. Yamaguchi, *Japan*
Co-chairman: Dr. Kiho Kim, *Republic of Korea*

8:15–10:15 a.m.

1.	Recent advance in chemotherapy of pulmonary tuberculosis	Dr. N. K. Menon *India*
2.	Atypical (opportunist) mycobacterial infections as a continuing problem	Dr. F. G. B. Edwards *Australia*
3.	Chemotherapy and the patient	Sister Mary Aquinas *Hong Knog*
4.	Primary drug resistance in Australia	Dr. A. G. McManis *Australia*
5.	Problems of drug default in domiciliary treatment	Dr. S. P. Pamra *India*

10:15–10:45 a.m. COFFEE BREAK

10:45–12:30 a.m. PANEL DISCUSSION

Chemotherapy of pulmonary tuberculosis in the countries of the Eastern Region

Moderator: Dr. N. K. Menon *India*
Reportors: Dr. K. Kameda *Japan*
Dr. C. C. Chang *Republic of China*
Dr. William Chan *Singapore*

6. Chemotherapy in Japan — Dr. K. Kameda *Japan*
7. Chemotherapy in Taiwan — Dr. C. C. Chang *Republic of China*
8. Chemotherapy in Singapore — Dr. William Chan *Singapore*

Discussers:

Dr. Nadda Sriyabhaya (9) *Thailand*
Dr. Yong Chul Han *Republic of Korea*
Dr. K. Kameda *Japan*
Dr. A. G. McManis *Australia*
Dr. William Chan *Singapore*
Dr. T. Y. Tseng *Republic of China*

Tuesday afternoon

Chairman: Dr. A. G. McManis, *Australia*
Co-chairman: Dr. Sulastomo, *Indonesia*

1:30– 3:00 p.m.

10. Treatment of pulmonary tuberculosis with ethionamide, cycloserine and pyrazinamide in Hong Kong — Dr. P. A. L. Horsfall *Hong Kong*
11. Ethambutol in the retreatment of pulmonary tuberculosis — Dr. K. V. Krishnaswami *India*

12.	Management of drug failure cases	Dr. H. B. Dingley *India*
13.	Management of drug failure cases	Dr. S. K. Basu Chaudhury *India*
14.	Management of drug failure cases	Dr. M. L. Mehrotra *India*
15.	A follow-up study of pulmonary tuberculosis patients found in the previous tuberculosis prevalence surveys	Dr. T. Nakajima *Japan*

3:00– 3:30 p.m. COFFEE BREAK

3:30– 5:30 p.m. PANEL DISCUSSION

Second-line drugs and pulmonary tuberculosis in the countries of the Eastern Region

Moderator: Sister Mary Aquinas, *Hong Kong*
Discussers:

Dr. T. Nakajima	*Japan*
Dr. Sung Chin Kim	*Republic of Korea*
Dr. Haji Megat Khas	*Malaysia*
Dr. S. P. Yang (16)	*Republic of China*
Dr. Le Van Giat	*Vietnam*
Dr. H. B. Dingley	*India*
Dr. Ki Yong Lee	*Republic of Korea*
Dr. K. T. Luh (17)	*Republic of China*

November 18, 1970

Wednesday morning

Chairman: Dr. Wong Hin Sun, *Singapore*
Co-chairman: Dr. Y. Yamamoto, *Japan*

8:15–10:00 a.m.

18.	How effective are the present control measures recommended for rural area	Dr. J. L. Bhatia *India*
19.	Evaluation of the results of smear examination by health workers in Health station	Dr. Y. C. Tsu *Republic of China*
20.	A critical appraisal of the relative merits of radiology and bacteriology in case-finding	Dr. S. P. Pamra *India*
21.	Compulsory community chest X-ray surveys in the tuberculosis case-finding program	Dr. R. S. A. Marshman *Australia*
22.	Four different approaches of case-finding in an aborigine area of Taiwan	Dr. T. Y. Tseng *Republic of China*

10:00–10:30 a.m. COFFEE BREAK

10:30–12:30 a.m. PANEL DISCUSSION

Case-finding methods in the countries of the Eastern Region

Moderator:	Dr. J. S. Sodhy	*Malaysia*
Reportors:	Dr. S. Sakamoto	*Japan*
	Dr. Wong Hin Sun	*Singapore*
	Dr. S. W. Luan	*Republic of China*

23.	Case-finding in Japan	Dr. S. Sakamoto *Japan*
24.	Case-finding in Singapore	Dr. Wong Hin Sun *Singapore*
25.	Case-finding in Taiwan	Dr. S. W. Luan *Republic of China*

Discussers:

Dr. J. L. Bhatia	*India*
Dr. Cotter Harvey	*Australia*

Dr. Hae Won Pyon	*Republic of Korea*
Dr. S. P. Pamra	*India*
Dr. S. Sakamoto	*Japan*
Dr. Wong Hin Sun	*Singapore*
Dr. C. C. Lin (26)	*Republic of China*
Dr. Boonsong Sunakorn(27)	*Thailand*

Wednesday afternoon

2:00– 5:00 p.m. FIELD TRIP

1. Visit Health Stations in the rural area
2. Visit Palace Museum
3. Visit the Veterans General Hospital

November 19, 1970

Thursday morning

Chairman: Dr. Jay Q. Lee, *Republic of Korea*
Co-chairman: Dr. Le Ven Giat, *Vietnam*

8:15–10:00 a.m.

28.	BCG vaccination by multiple puncture method employed in Japan	Dr. T. Sawada *Japan*
29.	Comparsion of multiple puncture and intradermal methods in the post-vaccination tuberculin allergy level	Dr. Y. Azuma *Japan*
30.	Studies on post-vaccination reactions in school children vaccinated with liquid and freeze-dried BCG vaccine	Dr. W. C. Chou *Republic of China*
31.	Epidemiological study of abnormal BCG scars among school children	Miss H. C. Chu *Republic of China*

10:00–10:30 a.m. COFFEE BREAK

10:30–12:30 a.m. PANEL DISCUSSION

BCG vaccination in the countries of the Eastern Region

Moderator:	Dr. C. W. Chao	*Republic of China*
Reportors:	Dr. Y. Azuma	*Japan*
	Dr. C. W. Chao	*Republic of China*
	Sister M. Aquinas	*Hong Kong*

32. BCG vaccination in Japan	Dr. Y. Azuma *Japan*
33. BCG vaccination in Taiwan	Dr. C. W. Chao *Republic of China*
34. BCG vaccination in Hong Kong	Sister M. Aquinas *Hong Kong*

Discussers:

Dr. N. C. Sen-Gupta	*Singapore*
Dr. Dal Ho Song	*Republic of Korea*
Dr. Y. Azuma	*Japan*
Sister M. Aquinas	*Hong Kong*
Dr. W. C. Chou (35)	*Republic of China*
Dr. S. P. Pamra	*India*
Dr. R. N. Roy	*Malaysia*
Dr. Gwyn Howells	*Australia*
Dr. Boonsong Sunakorn (36)	*Thailand*
Dr. T. Sawada,	*Japan*

Thursday afternoon

Chairman: Dr. the Hon. Dhun Ruttonjee, *Hong Kong*
Co-chairman: Dr. Arumainayagam Selvaratnam, *IUAT*

1:30– 3:00 p.m.

37. KAP survey on tuberculosis	Dr. Nak Chin Chung *Republic of Korea*

38.	Changes in prevalence and incidence of pulmonary tuberculosis	Dr. S. P. Pamra *India*
39.	Changing pattern of national TB association	Mr. B. M. Cariappa *India*
40.	The role of the womens' society played in anti-tuberculosis activities in Japan	Dr. M. Yamaguchi *Japan*
41.	Pilot Project in India	Dr. B. K. Shyam Singh *India*

3:00– 3:30 p.m. COFFEE BREAK

3:30– 5:30 p.m. PANEL DISCUSSION

Functions, fund-raising and health education problems of the voluntary organization of the countries of the Eastern Region

Moderator:

Dr. N. C. Sen-Gupta	*Singapore*

Reportors:

Dr. M. Yamaguchi	*Japan*
Dr. G. M. McManis	*Australia*
Mr. Jung Sun Sohn	*Republic of Korea*

Discussers:

Mr. B. M. Cariappa	*India*
Miss Sheila Iu	*Hong Kong*
Mr. Tae Kyu Kim	*Republic of Korea*
Dr. M. Yamaguchi	*Japan*
Miss P. Lu	*Republic of China*
Dr. Sun Kye Park	*Republic of Korea*
Dr. A. Selvaratnam	*IUAT*

November 20, 1970

Friday

FIELD TRIP

1. Visit Provincial Exhibition Hall at Taichung (8:00 a.m. by train)
2. Stay over-night at Sun Moon Lake

November 21, 1970

(Sun Moon Lake Hotel)

Saturday Morning

Chairman: Dr. S. K. Basu Chaudhury, *India*
Co-chairman: Dr. R. N. Roy, *Malaysia*

9:00–10:00 a.m.

42.	Early tuberculosis beginning with neurotic symptoms	Dr. Yun Kyu Park *Republic of Korea*
43.	A survey of the knowledge and attitude on tuberculosis in northern area of Taiwan	Mr. S. T. Wu *Republic of China*
44.	TB control and family planning program	Dr. M. L. Mehrotra *India*
45.	TB control and family planning program	Dr. Y. Rajashekhara *India*
46.	Decade of 70's, will it witness the global control of tuberculosis?	Mr. E. J. O'Brien *Canada*

10:00–11:00 a.m. PANEL DISCUSSION

Surgical treatment of pulmonary tuberculosis and TB Control

Moderator:

Dr. S. C. Chiang	*Republic of China*

Reportor:

Dr. P. Y. Wang	*Republic of China*

47.	Surgical treatment of pulmonary tuberculosis in Taiwan	Dr. P. Y. Wang *Republic of China*

Discussers:

Dr. H. B. Dingley	*India*
Dr. W. F. Cheng	*Republic of China*
Dr. William Chan	*Singapore*
Dr. J. S. Sodhy	*Malaysia*
Dr. S. K. Basu Chandhury	*India*
Dr. P. A. L. Horsfall	*Hong Kong*
Dr. A. Hara	*Japan*
Dr. M. Morimoto	*Japan*

11:00 a.m. CLOSING REMARKS Dr. J. S. Sodhy

LADY PROGRAM

Manager: Miss C. M. Ho

November 17, Tuesday

a.m. 9:00 Bus leaving Ambassador Hotel

9:20 Arriving China Pottery Factory to witness the process of making pottery and jade wares

10:30 Arriving National Yungmingshan Park, enjoy the natural beauty of the park

12:00 Lunch

p.m. 1:00-3:30 Shopping at down town Taipei

November 18, Wednesday

p.m. 2:00-5:00 Join the delegates to visit health station in rural area and the Palace Museum

November 19, Thursday

p.m. 2:30 Bus leaving Ambassador Hotel

3:30 Arriving King-Shan, vist the summer camp at sea-side.

4:30 Arriving Yeh-Liu, watch the fish-boats out to fishing against the colourful sun-set on the sea and the fantastic natural rocks in the evening sun-shine.

5:00 Leaving Yeh-Liu for Ambassador hotel

November 20, Friday

Join the delegates to Taichung tour and stay over-night at Sun-moon Lake.

ABSTRACT
SCIENTIFIC SESSION

1. Recent Adrance in Chemotherapy of Pulmonary Tuberculosis

Dr. N. K. Menon, India

The success of chemotheraphy has revolutionised the traditional approach to the treatment of pulmonary tuberculosis; orthodox beliefs and dogmas have given place to new concepts and practices, which have emerged from the findings of controlled clinical trials. Many of these controlled studies have been undertaken in developing countries and with a view to evolve economically feasible methods of chemotherapy for these countries. In my talk, this morning, I intend to review some of these new concepts and the supporting evidence from controlled clinical trials.

Sanatorium Vs Home Treatment

I would like to consider first, the most basic concept which concerns the importance of sanatorium treatment. It has been traditionally believed that prolonged bed-rest, high-protein calorie diet, good and airy accommodation etc., that is, the special virtues of sanatorium treatment are very important for success in treatment. That this is not so, has been proved beyond doubt by the findings of controlled clinical trials. The unique Madras Study which compared treatment in sanatorium with that at home on an outpatient basis with a standard regimen of PAS (Sodium) 10g. plus isoniazid 200 mg given in two divided doses a day for a year, has become a classic. It showed that there was little difference between the newly diagnosed patients treated in the sanatorium and at home both in their response at the end of a year of treatment (Tuberculosis Chemotherapy

Centre 1959) and in the occurance of relapses over a subsequent four-year period of follow up (Dawson et al, 1966). Also, there was no evidence that the dietary intake of the of the patients influenced the response to treatment (Ramakrishnan et al, 1961) or the occurance of relapse (Ramakrishnan et al, 1966) Furthermore, intensive follow-up of the close family contacts of the home and sanatorium treated patients, for a period of 5 years, demonstrated that the former were at no greater risk of developing the disease than the latter; indeed, the main risk to the contacts was before the index case was diagnosed and treatment started (Andrews et al, 1960 Kamat et al, 1966). Table 1. Summarises the findings.

Table 1. Tuberculosis Chemotherapy Centre, Madras
Summary of Home and Sanatorium Study

	Assessment	Home	Sanatorium
PATIENTS	Quiescent disease at 1 year	86%	92%
	Relapses over a 4-year period	7%	10%
CONTACTS	Cases of tuberculosis over a 5-year period	10%	14%

Favourable response at 1 year was attained by 86% of the home patients compared with 92% of the sanatorium patients. Relapse rates were 7% and 10% respectively.

Considering the contacts, the disease developed in 10% of the home and 14% of the sanatorium contacts.

The five year findings of this study prove that a good out-patient treatment is just as effective in newly-diagnosed patients and as safe to their close family contacts as a good sanatorium treatment. Thus, the most important factor in the treatment of tuberculosis is the chemotherapy the pati-

ent actually receives; the traditionally held virtues of sanatorium treatment are remarkably unimportant provided the patient receives adequate chemotherapy.

It may also be mentioned that there have been six other controlled trials reported in the total world literature which compared for 2—6 months, either sanatorium treatment with out-patient treatment (Tyrell, 1966; Bell, 1960; East Africa/British Medical Research Council, 1966) or bed rest with ambulation (Kay, 1957; Tuberculosis Society of Scotland, 1960; Wier et al, 1957; Wynn-Williams and Shaw, 1960) and none demonstrated any therapeutic superiority either of sanatorium treatment over out-patient treatment or of bed-rest over ambulation.

Thus, the evidence from all the controlled trials firmly establish the excellence of chemotharapy, to the virtual exclusion of all other factors, in the successful treatment of pulmonary tuberculosis. This new knowledge has made it possible to formulate a National TB Control Programme for the developing countries based on mass out-patient chemotherapy for all newly diagnosed patients.

Chemotherapeutic Regimens

Monotherapy with isoniazid alone

Isoniazid is the most effective, least toxic and least expensive of the anti-tuberculosis drugs, and a large body of medical opinion had held that isoniazid given alone is satisfactory chemotherapy for developing countries.

The merits of monotherapy with isoniazid alone was investigated in a controlled study in Madras. It compared 3 regimens of isoniazid alone with a standard regimen of isoniazid plus PAS in newly diagnosed patients with positive sputum. Table 2. Summarises the relevant findings.

Table 2. Tuberculosis Chemotherapy Centre, Madras
Isoniazid Study

Daily Dosages of Drugs, Efficacy and Complications

Regimens	Isoniazid		PAS (Sodium)		No. of doses a day	No. of patients	Bacteriologically quiescent disease at one year %	Peripheral neuropathy
	mg.	mean mg/kg	g.	mean g/kg				
Isoniazid plus PAS	200	4.4	10	0.22	2	90	91	1
Isoniazid alone	200	4.4	—	—	2	87	44	0
	400	8.8	—	—	2	68	58	9
	400	8.8	—	—	1	70	73	19

All the three regimens of isoniazid alone, namely, 200 mg and 400 mg, both given in 2 divided doses a day, and 400 mg given in a single dose daily proved unsatisfactory, success rates being 44%, 58% and 73% respectively. The dual-drug regimen of isoniazid plus PAS, on the other hand, proved highly effective, 91% of the patients attaining a favourable response at 1 year (Tuberculosis Chemotherapy Centre, 1960).

One other important finding from this study was that the therapeutic efficacy of isoniazid was related to its peak concentration in the serum attained in the day rather than to a continuous bacteriostatic level of the drug in the serum throughout the day (Gangadharam et al, 1961). This finding explains why patients who received the total daily dosage of 400 mg of isoniazid in a single dose responded substantially better than those who received the same dosage in two divided doses a day.

Subsequent studies in Madras (Tuberculosis Chemotherapy Centre 1963 a, b) showed that isoniazid alone in a higher single daily dose, namely, 650 mg. was no more

effective than a single daily dose of 400 mg.

In these studies, isoniazid neurotoxicity, principally peripheral neuropathy, occured in 19% of the patients who received isoniazid in a single daily dose of 400 mg (approximately 9 mg/kg body weight) and in 33% of those who received it in a single daily dose of 650 mg (approximately 14 mg/kg body weight). A double-blind study demonstrated that this could be prevented by the administration of pyridoxine, in as small a dose as 6 mg, with every dose of isoniazid.

There have been two more controlled studies of isoniazid alone in comparison with isoniazid plus PAS, one in East Africa (East African/British Medical Research Council Investigation, 1960 a) and the other in Morroco (Le Hir et al, 1964) in similar patients as in Madras. Both demonstrated that isoniazid alone was markedly inferior to isoniazid plus PAS in therapeutic efficacy.

All these studies prove beyond doubt that monotherapy with isoniazid alone is unsatisfactory for newly diagnosed patients with positive sputum; the minimum requirement of developming countries is dual-drug regimens.

Dual-drug regimens

PAS plus isoniazid: PAS (Sodium) 10 g. plus isoniazid 200 mg. given in two divided doses daily has been shown to be an effective oral form of combined chemotherapy in newly diagnosed patients. Thus, in the Madras Studies (Tuberculosis Chemotherapy Centre 1959; 1960; 1964; 1966) the proportions of patients attaining a favourable response at the end of a year of treatment with this regimen were 86%, 91%, 85% and 82%, that is, on an average, 86% of of the total 380 patients assessed in 4 separate studies. Similar results were obtained also in an East African Study

(East African/British Medical Research Council, 1963a), 85% of the 176 patients attaining a favourable response at 1 year.

The action of PAS in the PAS plus isoniazid regimen is said to be two fold, in part directly on the tubercle bacilli and in part by competition with isoniazid for acetylation and consequent increase in the effective serum isoniazid levels (Johnson & Corte, 1956; More et al, 1956; Mandel et al, 1956; Grosset et al, 1958). The Madras studies showed that concomitant administration of PAS does increase isoniazid serum levels (Gangadharam et al, 1961; Tripathy, 1969) but the direct action of PAS on the bacilli is therapeutically much more important.

Thioacetazone plus isoniazid: Investigations in East Africa (East Africa/British Medical Research Council, 1960 b; 1963) to find an inexpensive substitute for PAS resulted in the evolution of a standard oral regimen of thioacetazone plus isoniazid. The regimen consisting of thioacetazone 150 mg plus isoniazid 300 mg given in a single dose daily proved to be as effective and of the same order of toxicity in African patients, 83% and 78% of the patients, respectively, attaining a favourable response at the end of a year of treatment. The same two regimens were compared also in Madras and 82% of the patients on both regimens attained a favourable response at 1 year (Tuberculosis Chemotherapy Centre, 1966). Similar favourable results have also been reported from other parts of India (Deshmukh, Master and Kulkarni, 1963; Sikand, Goyal and Mathur, 1964; Menon, 1965). The regimen is now widely used in India.

The dosages of both the drugs are critical, lowering the dosage of either lowers the efficacy of the regimen (East Afria/British Medical Research Council, 1963). Also, increasing the dosage of isoniazid from 300 mg to 450 mg does not increase its efficacy (East Africa/British Medical

Research Council, 1966).

Thioacetazone plus isoniazid combination has the advantages that it is relatively inexpensive, small in bulk and easy to administer. However, side-effects and toxicity to thioacetazone shows wide geographical variations (Miller et al, 1966). In the Madras Study, major toxic manifestations which required either an interruption or termination of the regimen occurred to a similar extent, namely in 12% in the thioacetazone and in 11% in the PAS regimens. However, of the 75 patients in the thioacetazone series, 1 developed Stevens-Johnson Syndrome and 3 others exfoliative dermatitis. Also, minor side effects occured much more frequently in the thioacetazone regimen than in the PAS regimen. In a controlled study in Hong Kong (Hong Kong/British Medical Research Council 1968) 75% of the patients treated with thioacetazone regimen had a favourable response at one year compared with 82% of the patients treated with PAS plus isoniazid. However, side-effects including major toxicity occurred in 57% in the thioacetazone series including 14% who had the regimen changed due to toxicity compared with 21% and 1% respectively in the PAS series. Also in a controlled study in Singapore, major side-effects and toxicity occured in 43% of the patients on thioacetazone plus isoniazid regimen including 27% in whom the regimen had to be changed. (Supramaniam and Ridell, 1969)

Streptomycin plus isoniazid: Daily streptomycin injection plus oral isoniazid is the most effective of the two-drug regimens in the chemotherapy of newly diagnosed patients. Thus, in a British Medical Council (1955) study of streptomycin 1 g. plus isoniazid 200 mg. daily, 97% of the 60 patients assessed at 6 months had become culture negative. Similarly, in a U.S. Veterans Administration Study of streptomycin 1 g. plus isoniazid 300 mg. daily, 96% of the

52 patients assessed at 8 months and 97% of 32 assessed at 12 months had converted bacteriologically. Also, in a recent Singapore Study (Supramaniam and Riddell, 1969), a regimen of streptomycin 1 g. plus isoniazid 300 mg. daily given for 6 months resulted in a favourable response in 99% of the 69 patients assessed at 6 months.

Two-phase chemotherapy

Success of chemotherapy depends upon prevention of emergence of drug resistance. Emergence of drug resistance is a phenomenon related to the size of the bacillary population at the start of chemotherapy; the larger the size of the total population the greater the risk of emergence of drug resistance during the early phase of chemotherapy. It therefore follows that, during the early phase of treatment when the risk of emergence of drug resistance is highest, chemotherapy should be intensive with two or more of the most potent drugs.

These biological considerations have given rise to the concept of two-phase chemotherapy. After the initial intensive phase, when the bacillary population is reduced to such an extent that it no longer contains drug-resistant mutants less intensive chemotherapy can safely be used as continuation treatment.

Value of streptomycin supplement in the initial phase of chemotherapy

There is clear evidence from controlled trials that an initial supplement of daiy streptomycin substantially enhances the efficacy of the dual-drug regimens of PAS plus isoniazid, and thioacetazone and isoniazid.

Table 3. Controlled Studies of the Value of Streptomycin Supplement in the Initial Phase of Chemotherapy

Study	Regimen	Duration of supplement	Assessment made at:	Patients		Level of significance
				Total assessed	Un fav. response	
B.M.R.C. (1962)	SPH/PH	6 weeks	1 year	70	3	P=0.02
	PH	—		81	16	
U.S.V.A. (MacDonald 1968)	SPH/PH	6 weeks	8 months	241	12	P=0.04
	PH	—		217	20	
E.A/BMRC 1966	STH/TH	2 months	1 year	162	10	P=0.01
	TH	—		181	21	
IUAT (1969)	STH/TH	4 weeks	1 year	136	5	P=0.005
	TH	—		105	17	

Table 3 summarises the findings of 3 separate studies. In the British Medical Research Council (1962) Study an initial supplement of streptomycin to PAS plus isoniazid for the first 6 weeks reduced the proportion of patients with an unfavourable response at 1 year from 16% to 3%. The U. S. Veteran's Administration Study (MacDonald 1968) showed a reduction in the proportion of patients with an unfavourable response at 8 months, from 20% to 12%. The East African Study, (East African/British Medical Research Council, 1966) showed that an initial supplement of daily streptomycin for 2 months to thioacetazone plus isoniazid reduced the occurance of unfavourable response at 1 year from 21% to 10%. Finally, an International Union Against Tuberculosis (1969) investigation found that four-week daily streptomycin supplement to thioacetazone plus isoniazid reduced the proportion of patients with unfavourable response at 1 year from 17% to 5%.

A subsequent East African Study (East African/British Medical Besearch Council 5th Thioacetazons Investigation, 1970) investigated whether daily streptomycin supplement, for a shorter duration, namely two weeks or four weeks, would be as effective as 8 weeks. It was found that favourable response was attained by 88% of 147 patients who received no streptomycin supplement compared with 90% of 161, 94% of 159 and 96% of 162, of those who received it for 2 weeks, 4 weeks and 8 weeks, respectively, a statistically significant trend. There was also evidence from the monthly culture results and emergence of drug resistance to isoniazid and thioacetazone that, an initial streptomycin supplement for four weeks was somewhat less effective and a two-week supplement even less effective than the eight week supplement.

We know from accumulated clinical experience that triple-drug therapy with daily streptomycin plus PAS plus isoniazid for the first 6 months followed by PAS plus isoniazid is virtually cent per cent effective in newly diagnosed patients with drug-sensitive bacilli. The high efficacy of the regimen was also demonstrated in an IUAT (1964) Study. It showed that, of the 581 patients with drug-sensitive bacilli treated with the regimen, there were only seven (1.2%) who could be considered as failures including 5 patients who died wishin eight weeks.

None of these findings, however, lead to the conclusion that, for the initial intensive phase any three drug combination is superior to any two drug combination. It is possible that the superior results obtained with the initial triple-drug therapy might have been due to the fact that it contained a highly effective two-drug combination of daily streptomycin plus isoniazid.

Intermittent Chemotherapy

I would now like to consider a relatively new and

an entirely different concept—the concept of intermittent chemotherapy. Intermittent chemotherapy has definite advantages over daily chemotherapy; it enables the administration of every dose of the drugs under direct supervision and, thus, permits a precise knowledge of, and greater control over, the chemotherapy the patient actually receives. In addition, it would result in a reduction of the quantity of the drugs to be used and, therefore, of the cost of treatment as well as toxicity.

It has been generally believed that the maintenance of a continuous bacteriostatic level of the drugs in the serum ensured optimum therapeutic efficacy and, for this reason, the total daily dosage of the oral drugs is generally prescribed in 2, 3 or even 4 divided doses in the day. That this concept is not true in the case of isoniazid was shown by the Madras Study in which the peak serum concentration of isoniazid attained in the day played a more imporatnt role in response to treatment than maintenance of a continuous inhibitory concentration of the drug throughout the days. This finding gave a rational basis for controlled clinical trials of intermittent chemotherapy, in Madras.

The first study was a comparison of a fully supervised twice-weekly regimen of streptomycin plus high dosage isoniazid orally, and a standard daily oral regimen of PAS plus isoniazid. Table 4. shows the regimens.

Table 4. Tuberculosis Chemotherapy Centre, Madras
Intermittent Chemotherapy Study

Regimens

Regimen	SHTW	PH
Drugs and dosages	Streptomycin 1g plus Isoniazid, 14 mg/kg	PAS (Sodium), 220 mg/kg plus Isoniazid, 4.5 mg/kg
Rhythm	Twice a week together.	Daily in two doses

The twice-weekly regimen (SHTW) consisted of streptomycin 1 g., by injection, plus isoniazid 14 mg/kg body weight (i.e. 650 mg for a patient weighing 100 lbs) orally, given together twice-a-week. The control regimen consisted of PAS (Sodium) 10 g. plus isoniazid 200 mg., in two divided doses a day. The results assessed at 1 year are shown in Table 5.

Table 5. Tuberculosis Chemotherapy Centre, Madras
Intermittent Chemotherapy Study
Status At 1 Year

	SHTW	PH
Favourable response	94%	85%
Active disease	3%	14%
Death from TB	3%	2%
Total patients	72	66
Toxicity	0	3
Unco-operativeness	7	1
Non-tuberculous death	0	1
All patients	79	71

Favourable rersponse was attained by 94% of the patients on the twice-weekly regimen compared with 85% on the daily regimen. Thus, the twice-weekly regimen proved to be at least as effective as the daily regimen. Furthermore the relapse rates over a subsequent 4-year period of follow-up were also similar in the two groups.

This twice-weekly regimen is now being increasingly adopted in different parts of the world (usually after

an initial intensive daily phase) (Pool & Stradling, 1965; Dawson, 1966; Sparbaro & Johnson, 1967; Stradling, 1968; Polansky, 1969) as an alternative to unsupervised daily regimens.

The encouraging results of the twice-weekly regimen led to an investigation of the principles of once-weekly chemotherapy. In this study, 3 basically once-weekly regimens were compared with the twice-weekly regimen.

Table 6. Madras Study of Once-weekly Chemotherapy Regimens

Regimen	Streptomycin (g)		Isoniazid	Pyrazinamide	Rhythm
	High	Low			
SHTW	1	0.75	15 mg./kg	—	Twice-weekly
SHOW	1	0.75	15 mg./kg	—	Once-weekly
SHZOW	1	0.75	15 mg./kg	90 mg./kg	Once-weekly
SH/SHOW	1	0.75	400 mg.	—	Daily (4 weeks)
	1	0.75	15 mg./kg	—	Once-weekly (48 weeks)

The first is the control regimen (SHTW) in which streptomycin either 1 g. or 0.75 g. plus isoniazid 15 mg/kg body weight were given together twice-weekly. The next regimen (SHOW) consisted of the same drugs in the same dosages but given only once-weekly. The third regimen (SHZOW) contained, in addition, a third drug pyrazinamide in a dosage of 90 mg/kg body weight, all the three drugs given together once weekly. In the fourth regimen (SH/SHOW), streptomycin in the same dosages plus isoniazid 400 mg. in a single dose were given daily for the

first 4 weeks and this was followed by once-weekly streptomycin plus isoniazid. Table 7. shows the results at 1 year.

Table 7. Madras Study of Once-weekly Chemotherapy Quiescent Disease At 1 Year

Regimen	Patients with quiescent disease			
	Isoniazid inactivation rate		Streptomycin dosage	
	Slow %	Rapid %	Hign (1 g.)%	Low (0.75 g.)%
SHTW	97	91	94	96
SH/SHOW	95	76	92	84
SHZOW	87	53	72	78
SHOW	76	56	69	63

The twice-weekly regimen proved yet again to be highly effective, 95% of the patients attaining a favourable response at one year. The once-weekly regimen proved unsatisfacsory and addition of pyrazinamide to it did not substantially improve the efficacy, favourable response being 66% and 75%, respectively. On the other hand, when the once-weekly streptomycin plus isoniazid was supplemented by an initial intensive daily phase of streptomycin plus isoniazid for 4 weeks, favourable response was attained by 88% of the patients. Incidentally, this also demonstrates once again the striking efficacy of daily streptomycin plus isoniazid.

All the patients in this study had their isoniazid inactivation rate determined.

Table 8 shows the influence of isoniazid inactivation rate on response to treatment.

Table 8. Madras Study of Once-weekly Chemotherapy Status At 1 Year

(based on cultures at 10, 11 and 12 months)

Status of disease	SHTW	SH/SHOW	SHZOW	SHOW
Favourable response	95%	88%	75%	66%
Active disease	4%	12%	23%	32%
TB death	1%	0%	2%	1%
Total patients	97	101	101	77

Isoniazid inactivation rate had little effect on response to treatment with the twice-weekly regimen. On the other hand, in all the other three regimens the response was substantially inferior in the rapid inacsivators. In the SH/SHOW regimen, 95% of the slow inactivators had a favourable response compared with only 76% of the rapid inactivators, a substantial and significant difference. These findings show that on moving from twice-weekly to once-weekly chemotherapy isoniazid becomes inadequate in the rapid inactivators.

The next study was undertaken so determine whether addition of a third drug PAS would overcome the isoniazid inadequacy in rapid inactivators. PAS was chosen as the third drug because, apart from its anti-bacterial effect, it is said to enhance the serum level of isoniazid. Further, in order to determine whether differences in the once-weekly dosage of isoniazid would influence the therapeutic response, half the patients were given a dosage of 13 mg/kg and the other half 17 mg/kg in the once-weekly phase, so that the average dosage was 15 mg/kg as in the previous study. Finally, in order to obtain conclusive evidence on the relative efficacies of the two streptomycin dosages, half the

patients were given 0.76 g. and the other half 1.g. Table 9. shows the two regimens compared.

Table 9. Madras Study of Two Once-weekly Regimens

Rhythm and duration	Drug	SH/SHOW	SPH/SPHOW
Daily for first 4 weeks	Strep.	0.75 or 1 g.	0.75 or 1 g.
	Isoniazid	400 mg.	400 mg.
	PAS (Sod.)	—	6 g.
Once weekly for 48 weeks	Strep.	0.75 or 1 g.	0.75 or 1 g.
	Isoniazid	13 or 17 mg/kg.	13 or 17 mg./kg
	PAS (Sod.)	—	6 g.

The SH/SHOW regimen of the previous study is the control. The test regimen, SPH/SPHOW, is the same as the SH/SHow regimen except that, in addition to streptomycin and isoniazid, PAS (Sodium) in a dosage of 6 g. was also given both in the daily and in the once-weekly phase. Table 10. shows the results at 1 year.

Table 10. Madras Study of Two Once-weekly Regimens Favourable Response At 1 Year

Isoniazid inactivation rate.	SH/SHOW		SPH/SPHOW	
	Total patients	Bact. quiescence	Total patients	Bact. quiescence
Rapid	67	72%	72	76%
Slow	109	93%	98	95%
Both groups	176	85%	170	87%

Of the 67 rapid inactivators in the SH/SHOW regimen, 72% had a favourable response at 1 year compared with 76% of 72 in the SPH/SPHOW regimen, a very trivial difference.

Thus, addition of PAS did not improve the efficacy of the regimen in the rapid inactivators. In the slow inactivators, the SH/SHOW regimen proved yet again to be of high efficacy and addition of PAS resulted in little extra benefit, the favourable response being 93% and 95% respectively.

Similarly, increasing the once-weekly dose of isoniazid from 13 mg/kg to 17 mg/kg was of little benefit, favourable response being 71% and 79%, respectively, in the rapid inactivators, and 93% and 94%, respectively, in the slow inactivators.

To summarise, both the regimens proved to be of high efficacy in the slow insctivators and of substantially lower efficacy in the rapid insctivators. In other words, neither the addition of PAS nor increasing the once-weekly dose of isoniazid succeeded in overcoming the inadequacy of isoniazid in the rapid inactivators.

In order to determine the influence of serum isoniazid concentrations on response to treatment with the once-weekly regimens, serial serum isoniazid concentrations were determined in a total of 120 patients in this study, each of whom was given a once-weekly dose of the drugs. Both the peak concentration and the duration of coverage with a minimum inhibitory concentration of isoniazid were lower in the rapid inactivators than in the slow inactivators. It is of interest to know whether the lower peak concentration or the shorter duration of coverage accounted for lowering of the efficacy of the regimen.

Table 11. Madras Study of Two Once-weekly Regimens
Duration of Coverage (Hours)
With 0.2 ug/ml Isoniazid

Isoniazid inactivation rate	Regimen		Isoniazid dosage	
	SH/SHOW	SPH/SPHOW	Low (13 mg/kg)	High (17 mg/kg)
RAPID	14	15	14	15
SLOW	30	31	29	31

Addition of PAS resulted in the elevation of the peak concentration of isoniazid by 35% in the rapid inactivators i. e. to the level attained by the slow inactivators not receiving PAS. But yet, the response of these rapid inactivators was substantially lower than that of the slow inactivators being 76% and 93% respectively. It may, therefore, be concluded that peak concentration was not an important factor in response to treatment in the once-weekly regimen.

With regard to coverage, addition of PAS increased the duraton of coverage in the rapid inactivators only from 14 hours to 15 hours, as against 30 hours in the slow inactivasors not receiving PAS. Since the favourable response rate in the two groups was 76% and 93% respectively it may be concluded that duration of coverage is an important factor in response to treatment.

Similarly, increasing the weekly isoniazid dose from 13 mg/kg to 17 mg/kg elevated the peak concentration of the rapid inactivators by about 35% i.e. to the level attained by the slow inactivators receiving 13 mg/kg. However, the duration of coverage was increased only by an hour i.e. from 14 hours to 15 hours.

These findings show that the failure to improve the efficacy of the regimen in the rapid inactivators is mainly

due to the fact that neither addition of PAS nor increasing the dose of isoniazid succeeded in increasing the duration of coverage adequately.

Optimum duration of chemotherapy

Findings of controlled clinical trials (Velu et al 1961 a; Dawson et al; 1966; British Medical Research Council 1962) show that chemotherapy for two years is adequate for newly diagnosed patients and that chemotherapy beyond 2 years does not confer any extra benefit. In the Madras Studies in which chemotherapy was limited to one year and was with isoniazid either alone or with PAS, thioecetazone or streptomycin, the relapse rates over a subsequent four-year period of follow up was of the order of 15%. There was also clearcut evidence from a Madras Study (Nazareth et al 1970) that the total extent of radiographic lesions on admission to treatment and of the residual lesions at one year, and the speed of sputum conversion in the first year influenced the likelihood of relapse. It is of particular interest that the presence or extent of cavitation on admission to treatment, or at 1 year (i.e. open negative syndrome) did not influence the likelihood of relapse. However, in patients with no residual cavitation at 1 year isoniazid alone 200 mg daily for a second year reduced the relapse rate to 2% while it was substantially less effectively in patients with residual cavitation even in a dosage of 400 mg. daily.

2. Atypical (opportunist) Mycobacterial Infections as a Continuing Problem

Dr. F. G. B. Edwards, Australia

Two important questions to be answered in the problem

of infections caused by opportunist mycobacteria are, firstly, how frequently are these cases encountered; secondly, what treatment is available?

Some information is obtainable about the world distribution of these infections, and this is discussed. In particular the documentation of cases in Western Australia since 1959 is presented and analysed. Of the latter, 96% were caused by strains belonging to Runyon's Group II and non-Avian strains of Runyon's Group III.

In the Western Australian population very few cases remained undetected, hence the reported rates were close to true incidence. The actual incidence of pulmonary disease due to Group II and Group III mycobacteria showed no really significant sustained rise or fall over the eleven year period. This was in contrast to pulmonary tuberculosis which steadily declined.

Such cases, although numerically small, are therefore likely to present a continuing challenge, particularly as treatment with all known anti-tuberculosis drugs (including ethambutol and rifampicin) appeared to be quite unpromising. Furthermore, the Western Australian strains showed an absence of correlation between sensitivity patterns as indicated by laboratory testing and the results of treatment with the various drugs used. Surgery was successful in some selected cases. In lymph node infections, chemotherapy was of no value, whereas surgical excision was permanently curative.

The prognosis of the disease in most patients with pulmonary involvement was not favourable, progression of the lesions being slow, though in some there were periods of spontaneous "arrest".

3. Chemotherapy and the Patient

Sister Mary Aquinas, Hongkong

Without chemotherapy, the management of infectious tuberculosis is now almost unthinkable. The all-absorbing nature of the bacteriological studies focuses major attention on the laboratory. Consequently, effective drug-regimens and schedules for forestalling resistant organisims can be programmed.

While the clinician recognises that the co-operation of the patient is vital for success, the latter is not always impressed that the clinician or his assistants are in fact, particularly interested in him. Unaware of the extensive behind-the-scenes laboratory control that may be in operation for his benefit, he tends to slip out of the picture before his treatment is completed.

It is suggested that if the patient as a person be given greater consideration the necessary co-operation will not be wanting.

4. Primary drug resistence in Australia

Dr. A. G. McManis, Australia

5. Problems of drug default in domiciliary treatment

Dr. S. P. Pamra, India

Modern antimicrobial drugs can give cent per cent sputum conversion if used judiciously and under ideal conditions. In many institutions in many countries in the

world however, there is a gap between the ideal and the actual results achieved. The main reasons for failure of domiciliary treatment appear to be irregularity in drug taking or giving up treatment prematurely by the patient. Even if free drugs are made available to patients and their distribution is made easy, drug default cannot always be eliminated.

Four hundred and fifty irregular and non-cooperating patients were investigated with a view to find out the real reason for drug default. False sense of complacency fostered by quick alleviation of symptoms or disbelief in diagnosis was the most important reason of default. The next in order of frequency were clash between the patients' working hours and the working hours of the clinic and dissatisfaction with treatment at the clinic. The implications of this study and the measures that can be adopted within the limited resources of clinics in developing countries with a view to reduce, if not eliminate, drug default are discussed.

6. Chemotherapy in Japan

Dr. K. Kameda, Japan

According to the nation-wide tuberculosis prevalence survey in 1968, the number of active tuberculosis in Japan is estimated at 1,530,000. Among them about 600,000 cases have been actually found and registered. About 160,000 cases are hospitalized, the remaining three fourths of all patients being treated domiciliarily.

Most of domiciliary patients are treated by general practitioners, who treat patient according to the standard method of chemotherapy described in the Manual of the

Treatment of Tuberculosis.

Expense of the treatment is covered by several sorts of health insurance and governmental fund for the Tuberculosis Control Law. A total of 1000 million dollars is allocated annually to the tuberculosis treatment by the Law, in the governmental tuberculosis budget, excluding those financed by the health insurance. Patient requests the help of the law submitting application with his medical certificate, which contains the bacteriological findings, X-ray film of the chest and other clinical records. In each Health Center there is a Tuberculosis Advisory Committee composed of five members of experts. If the request is approved by the Committee, almost all expense of treatment is covered by public fund. In the case of infectious patients, almost all expense for hospitalization is covered by the governmental fund.

As the planning of treatment of individual patients, three drugs combination with SM, INH and PAS is recommended at the start of original treatment not only for bacteriologically positive but also negative cases. Of course there are many cases treated with INH and PAS. At present Thioacetazone is not used in Japan, because we have bitter experience of severe side effects caused by its use soon after the discovery of the drug.

We have made clinical studies of regimens such as SM+1NH+EB and Rifampicin+1NH+SM as the original treatment to find their curative effect excellent. However, such secondary drugs are practically not used for original treatment, with the exception of cases in which primary resistance for SM INH was found.

The chemotherapy is usually continued for six months or one year after attaining therapeutic target point.

The rate of defaulter averages 30—40% in one year of the domiciliary treatment. The rate is lower in initially infectious and symptomatic cases. We have no good policy to prevent the defaulter. The education of patients and home visiting by public health nurses are the only procedures for the prevention of defaulter. For the failure case of primary drug treatment, various combinations of secondary drugs are used also financed by the fund of the Tuberculosis Prevention Law and health insurance.

Many clinical cooperative studies on the effect of various combinations of secondary drugs have been carried out.

The rate of negative conversion of sputum was almost the same, nearly 80%, between various three-drug combination such as KM+TH+EB, KM+TH+CS, TH+EB+CS. In two-drug combination it was about 40—50%, TH+CS and EB+CS being somewhat inferior to TH+EB. If only one secondary drug is used, the conversion rate is about 20% or so. In the chemotherapy with secondary drugs on cavitary cases, radiological improvement is little and the relapse rate is rather high even in cases of negative conversion. Such cases are usually indicated surgical treatment, if possible, at an early stage after negative conversion. A combination of SM—PAS—INH for at least six months was tried out in cases of primary resistance to any of SM, PAS or INH.

The results showed that resistant cases were evidently inferior to susceptible cases both on the rate of negative conversion and improvement of X-ray finding at six months after treatment. The trend was especially remarkable in the cases found initially with a large amount of bacilli on culture and/or with two-drug resistance.

7. Chemotherapy in Taiwan

Dr. C. C. Chang, Republic of China

Chemotherapy for open cases

Starting from March 1957, the Government distributed INH to all infectious cases registered, From April 1959 to 1968 either INH with PAS or INH with streptomycin were supplied for a period of 12 months, followed by INH alone for the second year.

Mass Domicillary Chemotherapy Propram

A comprehensive tuberculosis control program for domicillary chemotherapy was carried out between August 1963 and January 1965. 4185 tuberculosis suspects were put on domicillary treatment under supervision. Drugs were distributed on monthly basis. Nearly 96% attended in the first month, declined to 80% subsequently. The average attending rate is 88%.

Intermittent Chemotherapy

A trial of acceptability of intermittent chemotherapy was carried out in Taiwan in 1966 to 1967, 2,298 tuberculous cases were put on this regimen, only 1,483 (64.5%) were completed their treatment. The regularity was nearly 100%. The results of X-ray follow-up examination at one year, is as follows: Among 1,183 cases, 618 (52.1%) showed inprovement, 64 (5.6%) worsened. Among 1,022 cases, 773 were converted to negative after one year treatment. The conversion rate is 75.6%

How Effective are Chemotherapy?

The results of the sputum conversion rate of the registered cases after completion of 12 months' treatment

(1964-1968) are shown in table 1:

Table 1. Assesment of Chemotherapy by Bacteriological Criteria

Year	Sputum conversion %
1964	54.9
1965	51.5
1966	55.4
1967	55.5
1968	62.9

The Prevalence of Drug Resistance

In comparison of the results of the second prevalence survey (1962-63) and the third survey (1967-68) in Taiwan, the situation of drug resistance problem seems to be more serious year by year.

For the rate of primary drug resistance, in general, it is 18.1% (16/88) in the 2nd survey, and 39.3% (35/89) in the 3rd. For the rate of acquired drug resistance, it is 61.1% (22/36) in the 2nd survey, and 71.0% (22/31) in the 3rd.

According to resistance to different drugs, there are 12 (13.6%) resistant to INAH, 10 (11.4%) to SM, and 2 (2.3%) to PAS. In the 3rd survey, There are 24 (27.0%) resistant to INAH, 26 (29.2%) to SM and 7(7.9%) to PAS.

According to resistance to number of drugs, in the 2nd survey, there are 8 (9.1%) resistant to one drug, 5 (5.6%) resistant to at least two drugs, and 3 (3.4%) to all three drugs. In the 3rd survey, 18 (20.2%) resistant to one drug, 12 (13.5%) to two drugs and 5 (5.6%) to three drugs.

The Role of TB_1 in Chemotherapy

A trial of side effects of thiacetazone to 206 eases was

done in 1968. Age were 31 to 50 years old. Most of them were cavitary. Among these 206 cases, 24 (11.7%) complained gastric disorder, 28 (13.6%) complained cutaneous disorder, 13 (6.3%) vestibular, and others, made a total of 76 cases (36.9%). Among those 76 cases, 45 (59.2%) had side effects within the first to fourth week, and those symptoms last about two weeks. 33 (15%) cases could not continue thiacetazone because of the side effects.

Two Important Points

According to the 2nd prevalence survey (1962) and the third prevalence survey (1967) there are two particular points of the problem of chemotherapy noticed in Taiwan.

1. The estimated number of infectious cases increased from 39,000 to 45,000 among the age group of 10 and over.
2. Drug resistance of Tubercle Bacilli among patients with history of chemotherapy showed low resistance to P. A. S.

The Importance of a Well Organized T. B. Program

Since T. B. control program is a nationwide problem, chemotherapy should be considered on the effectiveness of the regimen, acceptability and regularity. Effective supervision and patient cooperation are vital to the success of a chemotherapy program.

8. Chemotherapy in Singapore

Dr. William Chan, Singapore

National Tuberculosis Treatment Survey

The routine system for administering anti-tuberculosis

treatment is being investigated by assessing the bacteriological response at one year of the 3452 patients registered for treatment in 1969. A randomised controlled clinical trial is incorporated in this study, to select the more efficient of two fundamentally different approaches to treatment. One policy involves supervised administration of drugs throughout the year. the other depends principally upon selfadministration of the drugs by the patient. Results to date demonstrate a very high degree of success both in the population treated routinely in the national programme and in the sample of patients admitted to the controlled study of therapeutic policy.

The role of thiacetazone-containing regimens

Careful investigation of thiacetazone-containing regimens is necessary before introducing them widely into clinical practice. The efficacy and toxicity of a standard regimen of isoniazid plus thiacetazone (TH) was therefore compared to that of the same regimen supplemented with daily Streptomycin injections for twenty-six weeks (STH) and to that of a non thiacetazone-containing regimen of daily isoniazid plus streptomycin followed, at the end of 26 weeks. by isoniazid alone (SH/H).

Altogether 360 patients were submitted to the study. Of the patients adhering to the allocated regimens, the proportion with a favourable status bacteriologically at one year was 66% for the TH regimen, 100% for the STH regimen and 99% for the SH/H regimen. However, in the thiacetazone-containing regimens especially, drug toxicity was frequently encountered. If prolonged interruption of drug treatment on this account is assessed as an unfavourable response, then the proportion with a favourable status at one year was 61% for the TH, 84% for the STH and 97% for the SH/H regimen.

When toxicity and efficacy are thus considered together, the SH/H regimen appears clearly superior to both the other regimens at the end of one year.

Ethambutol as a companion drug to Isoniazid

The standard companion drug for Isoniazid in Singapore is sodium PAS. However this drug is poorly tolerated by many patients. As a possible substitute for PAS, the role of Ethambutol was investigated. Two regimens were studied, namely a standard regimen of daily Izoniazid plus PAS (P/H) and a trial regimen of daily Isoniazid plus Ethambutol the latter in a dosage of 25mg/Kg reduced, at the end of eight weeks, to 15mg/Kg (E/H).

One hundred and three patients were admitted to the trial. Of those assessed to date, favourable bacteriological response was obtained at one year was 91% in the E/H series and 87% in the P/H series. The proportion of patients with drug intolerance was 17% in the E/H series and 35% in the P/H series. The corresponding proportion with impairment of visual acuity was 9% and 14% respectively. Thus Ehambutol appears to be an effective and acceptable alternative companion drug to PAS. Its high cost in relation to PAS restricts its therapeutic role in routine practice.

9. Chemotherapy in Thailand

Dr. Nadda Sriyabhaya, Thailand

The general policy of chemotherapy of Thailand's TB Control Programme has been to expand the ambulatory treatment service. Starting in 1966 this is being achieved by integration of the control work into the basic health structure.

Planning of treatment of individual patient. The now universally accepted line is generally followed with two-phase regimen of chemotherapy with initial intensive phase of three first-line drugs (INH + streptomycin + PAS or INH + streptomycin + thiacetazone) for $1\frac{1}{2}$ to 3 months followed by oral two-drug regimen for up to $1\frac{1}{2}-2$ years. If the patient failed to convert the sputum after 6 months then a regimen of preferrably three reserved drugs would be contemplated, together with consideration for lung resection in case the lesion was extensive, although surgery has been done considerably less than 5-10 years ago before second-line drugs became available. It is felt that when there is still very limited choices of second-line drugs which are still very expensive then it is better to plan for early resectional surgery as in most instances it would be more difficult to follow-up patients on second-line drugs for a long period or 2 or 3 years, also considering that there would not be many drugs left to be used.

Mass treatment programme. Ambulatory treatment with inexpensive two drug regimen that is sufficiently effective from the control point of view that can be applied on a mass scale is the main policy. The regimen adopted for expansion to cover the whole country since 1965 is oral drugs of INH plus thiacetazone. It has been found that the latter is more toxic with more side effect than PAS among the population in this country, with intolerance to the drug ranging from 12–20%. For those who could not be continued on the drug only very limited supply of PAS is available. For nation-wide programme there is no solution in sight for the use of second-line drugs which are still very toxic or very expensive except to try to improve the efficiency of the primary treatment service.

Defaulters' problems. Although thorough study of the problems is still to be undertaken, it has been observed

that the causes of defaulting are more generally of socio-economic nature than to put the blame mainly on defective health education. Particularly in larger urban areas the attendance for treatment tends to be worse than in rural localities with fairly good basic health service. It appears that the defaulter rate tends to be less if the treatment can be set up at peripheral level, nearest to the patients' homes, where socio-economic conditions would be more homogenous than urban areas, namely, at the local (rural) health centers.

Primary drug resistance. This has been difficult to determine accurately because of the difficulty in obtaining true history of previous treatment. The main concern now is the widespread practice of improper drug usage; unsatisfactory regimen; insufficient period of therapy; irregular therapy; no effective control on the sales of drugs so that anyone could buy any drug and treat themselves. It has been found that 20–30% of patients attending the Central Chest Clinic for the first visit were excreting bacilli resistant to Isoniazid.

Intermittent chemotherapy. A limited trial of twice weekly streptomycin plus high dose of isoniazid was carried out since late 1968, at the Central Chest Clinic in Bangkok. It is rather disappointing to note that among 98 patients admitted to the trial, 15 asked to have the treatment changed to oral regimen, 4 of which because of toxicity to streptomycin. while the rest 11 were not able to attend the twice weekly injection. Of the 83 remaining only 56% were regular in their attendance up to a year. while 20% were lost and 24% were irregular. The causes of defaulting were again similar to oral daily regimen, that is, mainly socio-economical.

The use of second-line drugs. We have had only limited experience with a small number of patients on pyrazina-

mide + ethionamide. For 64 patients in our series the result was not very encouraging as almost one-third were lost, a large proportion because of toxicity or side-effect. The conversion rate was low, most likely less than 55%. This might be due to(1) low dosage with still considerable side-effect so that many patients might have not taken the drugs; (2) crossed resistance between ethionamide and thiacetazone, the latter having been used previously.

(regimens containing ethambutol are still under trial)

10. Treatment of pulmonary tuberculosis with Ethionamide, Cycloserine and Pyrazinamide in Hong Kong

Dr. P. A. L. Horsfall, Hong Kong

The paper describes the results of treatment of resistant cases using a basic regimen of ethionamide, cycloserine and pyrazinamide, Some 200 routine admission admitted during the period July, 1966 to June, 1967 were treated and followed up for 3 years.

11. Ethambutol in the Retreatment of Pulmonary Tuberculosis

Dr. K.V. Krishnaswami, India

Introduction:

The need for effective and minimally toxic drugs for the management of drug resistant cases is ever increasing. Reports from the world literature as also ours indicate that Ethambutol is one such drug.

The first study was undertaken to assess the therapeutic efficacy of and the side effects with Ethambutol in South Indian patients suffering from Chronic active Pulmonary Tuberculosis unresponsive to therapy with the Primary anti-tuberculous drugs. (SM, PAS and INH).

One hundred cases, admitted for the study, were radiologically matched and randomly allocated to the following two regimens:

TREATMENT REGIMEN

Ethambutol	–25 Mg. per Kg. daily for 60 days & Subsequently 15 Mg per Kg. daily	EMBH Single dose taken together.
Plus		
INH	300 Mg daily	
Thiacetazone	150 Mg.	TH Single dose taken together.
Plus		
INH	300 Mg.	

Of the 50 cases in each group, 17 had moderate lesions and 33 extensive lesions.

The pretreatment investigations viz., radiological bacteriological, biochemical and ophthalmic were repeated periodically.

Results:

At 6 months sputum conversion was 61% and 52% and radiological improvement was 67% and 52% in EMBH and TH group respectively.

Side Effects:

There was greater incidence of minor side effects in

the TH group. Visual complications and major side effects did not occur in both the groups.

Study No. 2

Comparison of Ethambutol and Pyrazinamide (EMBP) with Ethionamide and Pyrazinamide (ETHP) in the Re-treatment of Pulmonary Tuberculosis.

(Summary)

Since Ethionamide is one of the commonly used second line drugs, the efficacy of Ethambutol was evaluated with that of Ethionamide in the Retreatment of Pulmonary Tuberculosis,

132 cases, admitted for the study were readiologically matched and randomly allocated to the following two regimens:

TREATMENT REGIMEN

Ethambutol	25 Mg. per kg. daily for 60 days and subsequently 15 Mg. per Kg. daily.	EMBP Single dose taken together
Plus		
Pyrazinamide	1.5 Gm.	
Ethionamide	500 Mg.	ETHP. Single dose taken together
Plus		
Pyrazinamide	1.5 Gm,	

Of the 66 in each group 26 had moderate lesions and 40 extensive lesions.

Results:

At 6 months bacteriological conversion was 61% and 40% and radiological improvement was 89% and 60% in EMBP and ETHP group respectively.

Serious drug toxicity was not met with in both the groups. None of the cases in both the groups showed any evidence of Hepatic or renal dysfunction.

The minor side effectis were more often met with in the ETHP groups. No visual disturbance was seen in the EMBP group.

Conclusion:

The results of the above studies show that (1) very satisfactory sputum conversion and radiological improvements with Ethambutol, (2) Side effects are few and none of the cases developed any visual complications while on Ethambutol on the dosage schedule adopted and (3) In view of its ease of administration low toxicity and good efficacy patients acceptability is very good.

12. Management of Drug Failure Cases

Dr. H. B. Dingley, India

The incidence of drug failure or drug resistant cases is gradually diminishing in most of the economically developed countries where good primary chemotherapy is available but in many developing countries acquired drug resistance is fairly frequent.

The management of drug failure cases may be (i) specific treatment with the reserve drugs or second line drugs or (ii) surgical treatment with irrevocable collapse procedure e.g. Thoracoplasty operation or resective procedures.

Results of two clinical studies, with the use of second line drugs one with ethambutol and the other a controlled trial with ethionamide, pyrazinamide and cycloserine will be reviewed.

In the first pilot study of 66 patients with poly-resistant bacilli, 60 patients completed six months treatment, 3 died and 3 left against medical advice. Of these in 38 or 60.3% there was bacterial conversion by culture with associated radiological regression/clearance, but cavities were closed in 5 or 8.4% and became smaller in 28 or 47.4%

Of the remaining 22 patients, in whom the sputum was positive, 10 were still sensitive to ethambutol, in four sensitive studies for ethambutol could not be done and the rest eight had become resistent to ethambutol.

None of the patients showed any toxic effects except one who had complaints of blurred vision, which did not necessitate any interruption in treatment.

In the second controlled study 120 patients resistent to standard drugs were allocated at random to the three various drug regimens of ethionamide, pyrazinamide and cycloserine with isoniazid and para-aminosalicylic acid as a common drug.

The results of six months treatment with either of the above regimens showed that in group I with ethionamide and cycloserine, bacterial conversion was in 19 or 54.3%, group II with ethionamide and pyrazinamide it was in 19 or 61.3% and in group III with pyrazinamide and cycloserine in 16 or 51.6%.

Similarly radiological clearance and cavity closure was in 6 or 17.1% in group I, in 9 or 29% in group II, in 5 or 16.1% in group III. The cavities became smaller with radiological regression in 19 or 54.3% in group I, 14 or 45.1% in group II and 13 or 42% in group III.

Toxic symptoms were in four patients or 9% in group I, 3 or 8.1% in group II and 3 or 7.7% in group III respectively necessitating stoppage of treatment.

Of the 790 patients in whom thoracoplasty operation was done, 651 or 82.4% were with positive sputum. Of these 383 or 58.8% were with resistent bacilli and the sputum conversion was in 336 or 87.7% with radiological quiescence.

Similarly of the 291 pulmonary resections done for tuberculous pathology, 195 were with positive sputum and of these 93 or 47.7% were with resistent bacilli. Of these bacterial conversion was in 86 or 92.4%.

The merits and demerits of surgical treatment and the specific treatment will be presented particularly high lighting their economical and organisational aspect as could be recommended for a developing country.

13. Management of Drug Failure Cases of Pulmonary Tuberculosis

Dr. S. K. Basu Chaudhuri, India

Drug failure cases are those where available anti tubercular drugs have not been able to achieve arrest of the disease. They are:—

1. Sputum positive cases—mostly excreting drug resistant bacilli.
2. Sputum negative cases with permanent anatomical changes in the lung like—
   (a) Persistent cavitation
   (b) Destroyed lobe or lung
   (c) Gross tuberculous bronchiectasis.

It has been claimed that bacteriologic arrest can be achieved with first line drugs alone provided drugs are

taken in optimal regimens for prolonged period in religious regularity. But if for some reason the above criteria are not reached in the initial phase of the disease, drug resistance developes and/or some permanent anatomical changes take place in the lung tissue.

Causes of drug failure may be many but they may be grouped in two main headings as follows:—

1. Failure to prescribe the regimens of optimal chemotherapy due to lack of money for medical facilities in developing countries.
2. Failure on the part of the patient to take the drugs as prescribed for adequate length of time due to—
   (a) Unpleasant side effects
   (b) Forgetfulness
   (c) Indolence
   (d) Failure to understand instructions.

Some of the newer second line drugs like Ethambutol and Rifampicin are very good and powerful but they are not ordinarily available in a developing country like India. As a result quite a number of cases need surgical treatment. Occasionally argument is put forward that since there are so many reserve drugs available now, what is the need for surgery? The need for surgical treatment in India is due to:

1. Non availability of reserve drugs.
2. High cost of reserve drugs.
3. Unpleasant side effects and uncertain results.
4. Development of permanent changes in the lobe or lung like—
   (a) Persistant cavitation.
   (b) Destruction of lobe or lung.
   (c) Gross tubercular bronchietasis.

What problems do the drug failure cases present? Problems are two pronged namely for the patient and for the community. A drug failure case is more difficult to tackle by the physician and less likely to completely get rid of the disease as compared to a fresh case. For the community, the management of a drug failure case costs much more money and if they excrete drug resistent bacilli in the sputum, they are likely to infect people of a community with drug resistant bacilli ultimately involving a problem of very much greater magnitude.

What is the solution of this problem? In a developing country like India where the beds available for tubercular cases are small in number and number of patients is so large, it is very difficult. Our only hope lies in the prevention of getting a patient to a drug failure stage and this can only be achieved if the patients can be treated with optimal chemotherapy for prolonged period in disciplined regularity. Human nature as it is, this again is a very difficult target to reach with domiciliary treatment that we have to follow in our National tuberculosis programme. However there is no question of giving up hope—we have to have a happy coordination between institutional and domiciliary treatment programme and intensify the health education programme so that we make a dent in this vast health problem of nation wide character.

14. Management of Drug Failure Cases

Dr. M. L. Mehrotra, India

Since November 1968, 129 pulmonary tuberculosis patients who had failed to respond to standard anti-tubercular drugs and who had their sputum cultures resistant to at least one of the primary drugs isoniasid or streptomycin were

put on second line of treatment. These patients either had their pretreatment cultures resistant or showed resistance during the treatment period in our institution.

Anti-tubercular treatment, which a patient took before he came to our institution, has been carefully recorded.

The patients are being given 2 weeks supply of drugs at a time. At each visit patients are interrogated about self administration of drugs and regularity in drug intake. Any relevant complaints of the patients are also carefully noted at each visit.

Every patient is being followed with the same intensity. Sputum examination by direct smear and culture is being carried out at each visit of the patient. Bacteriological results at 1 month, 2 months & 6 months are being analysed and will be presented.

Weight of the patients is being recorded at each visit.

Radiological examination is being done at 6 months from the staff of second line treatment.

Patients have also been advised and referred for surgical treatment.

Attack rate of Tuberculosis amongst close contacts of these resistant cases is also being studied and would be presented at the Regional Committee meeting.

15. A Follow-up Study of Pulmonary Tuberculosis Patients Found in the Previous Tuberculosis Prevalence Surveys

Dr. T. Nakajima, Japan

A follow-up study of pulmonary tuberculosis patients, found in the Tuberculosis Prevalence Surveys in 1953 and

1958 was made first in 1964, and was repeated in 1968 on the same patients together with a follow-up of patients found in the 1963 Survey.

The present status of patients in 1968 was known in 76.2%, 81.3% and 87.3% of patients found in the 1953, 1958 and 1963 surveys, respectively.

The prognosis of tuberculosis patients might be expressed most simply by the survival rate and the mortality rate and the latter may be subdivided into tuberculosis death and non-tuberculous death. The proportion of the above three categories and its yearly changes during the follow-up period can well be expressed by using triangular diagramme.

Various factors might influence the prognosis of tuberculosis patients. In the present study, age, extent of pulmonary lesions and the bacteriologic status were analyzed in relation to the prognosis.

Fig. 1 shows the prognosis curve of patients found in 1953, 1958 and 1963.

Fig. 2 shows the prognosis curve of patients found in the 1953 Survey according to the age in 1953.

The prognosis curve of patients found in 1953 is presented in Fig. 3 according to the extent of pulmonary lesions.

The results of follow-up made on patients found in the previous three Surveys are presented in Tab. 1 according to the initial bacteriological status.

The prognosis of whole bacilli positive cases was clearly worse than that of bacilli negative cases. Dividing by the extent of pulmonary lesions, the prognosis of cases with far advanced cavitary lesions with negative bacilli was worse than that of the whole bacilli positive cases.

Tab. 1. Results of Follow-Up by Initial Bacteriological Status and NTA Claiiification*

Init. status		1953—1968			1958—1968			1963—1968		
Bact.	NTA	TB-death	active	cured	TB-death	active	cured	TB-death	active	cured
Total	Tot.	14.1	17.2	68.7	9.0	18.9	72.1	3.5	38.5	58.0
	F.A.	52.6	22.9	24.5	52.8	28.3	18.9	20.0	67.6	12.4
	M.A.	19.3	23.5	57.2	12.2	25.3	62.5	5.7	56.1	38.2
	Min.	11.4	22.3	66.3	1.2	15.2	83.6	0.7	29.2	70.1
Positive	Tot.	21.8	24.7	53.8	30.4	25.9	43.7	15.0	52.4	32.6
	F.A.	53.7	19.8	26.5	59.1	26.7	14.2	39.3	46.7	14.0
	M.A.	14.8	32.8	52.4	23.9	26.1	50.0	8.9	60.7	30.4
	Min.	8.1	10.6	81.3	6.9	24.6	68.5	4.5	47.8	47.8
Negative	Tot.	11.2	16.6	72.2	5.0	18.3	76.7	2.3	36.8	60.9
	F.A.	45.5	33.5	21.0	47.8	24.6	27.6	8.5	79.3	12.2
	M.A.	18.9	19.5	61.6	8.3	26.5	65.2	5.1	54.3	40.6
	Min.	1.8	14.6	83.6	1.0	15.1	83.9	0.6	28.4	71.0

* Figures are represented in %.

Comparing the prognosis of patients with the same extent of lesions found in 1953, 1958 and 1963, no marked difference was found in the prognosis of minimal cases, while in the case of far advanced type, the survival rate raised in patients found in later years. In the case of moderately advanced type, the prognosis was improved in patients found in later years. These facts indicate that many of minimal cases heal spontaneously without receiving treatment, while the prognosis of far advanced cases is generally unfavourable and difficult to improve, and the prognosis of moderately advanced cases has been improved in accordance with the advancement in chemotherapy and surgical treatment.

16. Chemotherapy on Tuberculosis

Dr. S. P. Yang, Republic of China

On the effect of TB chemotherapy, I have no slightest doubt that at the initial treatment, the combined prolonged use of so-called the first line drugs can achieve 85-95% of cure rate. I also do not doubt that even at the retreatment, the combined prolonged use of more than three kinds of so called second line drugs may achieve 80% of cure rate provided the patient can tolerate these drugs physically and economically. It is also generally agreed that the clinical effect of these chemotherapeutic drugs is most remarkable at the first couple of months, but unless some more effective bacteriocidal drugs come out and the treatment can be shortend to a few months, the prolonged use of effective drugs is essential. In our daily practice, however, only a minor portion of the patients who received initial treatment did complete the treatment. Therefore, to me, the most important things in the treatment of pulmonary tuberculosis is to have the patient complete the treatment successfully when he or she first receive chemotherapy.

For this reason, I would like to emphasize the following points in regards to the TB chemotherapy.

1. Closer clinical observation and follow-up chest x-rays during the first three months.

2. If the initial response is not satisfactory as expected, the reason should be found out, and if necessary the drug regime may be changed without delay.

3. If the initial response is satisfactory, the patients has to be persuaded to continue the same regime for sufficient period of time with regular follow-up of 3 months'

interval.

Now how to convince a patient with little symptoms to continue the treatment? I believe this is a matter of education both to the public and the medical professions and the voluntary agency such as TB association is most adequate to take care of this problem. Pamphlets, posters and leaflets on TB control or treatment should be revised to emphasize "modern concept" and may be distributed to the patients through local medical doctors in charge of them. The modern concepts must be taught at school and through mass communication media such as TV, so that they may become national common sense.

17. Retreatment of Pulmonary Tuberculosis with Secondary Antituberculosis Drugs

Dr. Kwen-Tay Luh, Republic of China

A great number of active chronic advanced pulmonary tuberculosis patients who have bacilli resistant to standard antituberculosis drugs cast one of our major public health problem in our community. The treatment of these patients is usually regarded as very difficult. The advance of second line drugs in recent years encourages us to carry out this study for purpose of evaluating the effect of these secondary antituberculosis drugs.

Two hundred and seventy cases who had received second line drugs medically for more than 6 months from 1961 to 1969 at Taipei Demonstration Center, Provincial Taiwan Tuberculosis Control Bureau, are analysed.

All of patients had advanced pulmonary tuberculosis, resistant tubercle bacilli to the first line drugs and failed

to respond to standard antituberculosis drugs. Nineteen patients had previous surgery for pulmonary tuberculosis.

The drugs included ethambutol, ethionamide, d-cycloserine, kanamycin, capreomycin, pyrazinamide and isoxyl. Isoniazid was continuously administrated regardless its susceptibility. The duration of treatment with secondary drugs in these cases ranged from 6 months to over 2 years after the initiation of treatment.

Bacteriologically, the sputum conversion rate by culture at 6 months in the one drug group was 44 per cent, in 2 drugs group 75 per cent, in 3 drugs group 88 per cent, in 4 drugs group 94 per cent respectively. Failure and reversion occured in 56 per cent of one drug group, 33 per cent of 2 drugs group, 11 per cent of 3 drugs group and 9 per cent of 4 drugs group.

Roentgenologically, most of them shows no change or only slight improvement because of presence of chronic extensive and irreversible lesions. Significant improvement after 6 months treatment was seen in 3 per cent of one drug, 14 per cent of 2 drugs, 24 per cent of 3 drugs and 11 per cent of 4 drugs group. Four patients of one drug group became worsened.

Untoward drug reaction developed in 6 per cent of one drug, 30 per cent of 2 drugs, 55 per cent of 3 drugs and 50 per cent of 4 drugs group.

Despite considerable drug toxicity, the result of this study shows that the concurrent use of multiple secondary drugs in the retreatment of severe pulmonary tuberculosis is rather promissing.

18. How Effective are the Present Control Measures Recommended for Rural Areas

J. L. Bhatia, India

1. India has accepted the "District TB Control Programme" as a comprehensive control programme for the whole country specially the rural areas.
2. This Programme was begun at Amritsar District in July 1967. This district is at a great advantage in TB Control in several important aspects as compared to many other districts in India.
3. An analysis was made of all consecutive pulmonary TB patients diagnosed at the district TB Control Centre Amritsar from November 1967 to June 68 when the TB Control Programme was well on its way. A total of 1050 cases was analyzed.
4. An overwhelming majority of cases had cough, weakness, fever and pain in the chest as their major symptoms.
5. Only 33% patients first presented themselves at primary health centres, govt. hospitals including the Medical College Hospital, and qualified medical practioners.
6. Majority of the patients (57.4%) presented themselves at the District TB Control Centre guided by ex-patients of this centre, by friends and relatives or on their own initiative but not by medical practitioners. 375 patients (35.7%) belonged to the rural areas of Amritsar.
7. During the same period only 6 cases were diagnosed by the primary health centres in the rural areas under the programme.
8. The diagnosis of tuberculosis was clinically suspected in only 21% of patients before they reported to the Dis-

trict TB Control Centre. The remaining 79% were given symptomatic treatment. A significant number (15.6%) was treated for Typhoid.

9. Even at the District TB Control Centre, where the laboratory personnel are highly trained sputum smear was positive in less than half (46.3%) of the patients.

10. Since the completion of this study in the two year period from June 1968 to June 1970, 35 more cases of pulmonary tuberculosis have been diagnosed in the rural areas. During the same period 5611 cases have been diagnosed at the District TB Control Centre Amritsar.

11. During the same period 361 patients have been taking treatment in the rural areas while 1314 have completed treatment and 2017 are still taking treatment at the District TB Control Centre Amritsar.

12. Very sincere efforts are continued to be made by a devoted staff to make the District TB Control programme a suocess in the rural areas. But it seems very doubtful if many of the sweeping assumptions made by the authors of the programme will ever materialize.

19. Evaluation of the Results of Smear Examination by Tuberculosis Health Workers in Health Stations

Dr. Y. C. Tsu, Republic of China

In order to strengthen the tuberculosis control program in Taiwan, two hundred high school graduates were employed as assistants in the rural health stations. They had received a two week training with emphasis on direct microscopic sputum examination. The method to assess the accuracy

of their sputum examination is as follows:

The test slides were prepared from 10-2, 10-3, 10-4, 10-5, dilutions of glycerin-egg-white containing tubercule bacilli and bacilli free solution. Five slides constitute a group, and each group contains one negative slide and 4 slides of different dilutions. These groups of slides were distributed to 103 health workers who were to be tested, while at the same time 19 experienced laboratory technicians from Tuberculosis Centers and Health Bureau were also tested for control.

The results showed that of the 98 tuberculosis health workers (exclude 5 with incomplete reports), 20 or 20.4% reported correctly on five known slides; 35 or 35.7% had one arror; 22 or 22.4% had two errors; 17 or 17.4% had 3 errors and 4 or 4.2% had four errors. The percentage of those health workers who reported correctly on 5 known slides (20.4%) was lower than the experienced laboratory technicians (42.1%). The causes of this results might be due to their limited experiences in both staining and microscopic reading, since they have carried out this program for only about 6 months. Efforts are being made to encourage them to collect more specimens and examine them to emprove this important work.

20. A Critical Appraisal of the Relative Merits of Radiology and Bacteriology in Case-Finding

S. P. Pamra, India

Efficiency of bacteriology and radiology in case-finding has been worked out from a study carried out by the New Delhi TB Centre in a population of 6000. Persons 15 years or more in age, numbering 3234, were questioned for cough

of 1 month or more in duration before they were x-rayed. All those with abnormal shadows in the miniature film were investigated and if sputum was negative, final diagnosis was based on 3—6 months observation with a view to exclude, as far as possible, the non-tuberculous and inactive tuberculous. The word case has been used in its broad sense; to include the active and presumably active (bacillary and abacillary) needing treatment.

Radiology alone is an undependable tool for case-finding. All the 59 'cases' in the in the population, 13 bacillary and 46 abacillary, could be found by supplementing radiology by bacteriology to retrieve 'under-diagnosis' and an observation period to eliminate 'over-diagnosis'. Bacteriology alone is authentic as far as it goes. By examining the of 371 'symptomatics' by direct microscopy half the bacillary cases (6 out of 13) could be easily discovered. Three more could be detected by making culture facilities available but nearly 120 specimens would have to be cultured for every positive result. The remaining 4 bacillary cases (about 30% of total bacillary cases) being asymptomatic would be missed.

If the 371 symptomatics were x-rayed first, the number of sputa to be examined would be reduced by two thirds and some additional asymptomatic cases would also be detected.

The cost of finding a case by various procedures, time taken therein and acceptability of treatment by cases so discovered have also been studied. If x-ray facilities are available, x-raying the symptomatics supplemented by sputum examination of those with abnormal x-ray findings appears to be the most rewarding case-finding procedure. Where x-ray facilities are not available, direct microscopy of the sputum of symptomatics can help to find all the highly infectious cases in the community easily, though not cheaply.

21. Compulsory Community Chest X-ray Surveys in the Tuberculosis Case Finding Programme

Dr. R. S. A. Marshman, Australia

In 1948 an Australia-wide campaign against tuberculosis was introduced, co-ordinated and financed by the Commonwealth Government. This is being successful and the death rates from all forms of tuberculosis have declined from 27.8 per 100,000 in 1948 to 2.0 per 100,000 in 1968, and notification rates of new cases from 46.3 per 100,000 to 14.6 per 100,000 in 1969. Mass Community Chest X-ray Surveys were chosen for the major role in case finding, and have been introduced into all States of Australia on a voluntary basis, or made compulsory for adults, using legislation under Health Acts. At present attendance is compulsory for adults in all States.

During a special voluntary survey in the State of Victoria, only two-thirds of the adult population were X-rayed despite concentrated publicity by all modern means. This contrasts with over 98% attendance using legal compulsion under the Health Act. The improved response was partioularly evident in persons aged over 50 years, where the incidence of active tuberculosis is almost three times higher than in younger adults.

Compulsory community-wide chest X-ray surveys are expensive and require many auxiliary conditions—appropriate legislation, nominal rolls of the population, means of mass communication and public education, a comprehensive tuberculosis programme with records and services, and trained personnel. These situations are not available in all countries, but where control programmes are sufficiently advanced, efficiently organized Compulsory Community

Chest X-ray Surveys are the quickest and most effective means of detecting unsuspected pulmonary tuberculosis, active or inactive, and so hasten control in that segment of the community which carries the highest risk of continuing the spread of tuberculosis.

22. Four Different Approaches of Case-Finding in an Aborigine Area in Taiwan

Dr. T. Y. Tseng Republic of China

The six tribal Shans are located in the mountain areas of the east coast with a population of 50,137 (36 villages). Except a few villages, most of it take one to six hours by walking from the local highway.

The results of the four different approaches of the case-finding are shown as the followings.

Table 1.
Cases Found by 4 Different Approaches by Locality

Place	Population	Open Cases Registered	Open Cases Detected by Mobile Clinic Rounds		
		Before May 1968	1st mobile X-ray clinic May 1968	2nd mobile X-ray clinic May 1969	3rd mobile X-ray clinic Dec. 1969
(Shan)			new case	new case	new & old case
Tajen	3,945	2	3	1	11 (6, 5)
Kinfon	2,947	6		2	10 (5, 5)
Enpin	3,693	6		7	44 (22, 22)
Haituan	4,004	1		8	8 (3, 6)
Tongho	19,336	32		4	44 (33, 11)
Changpin	16,212	10		10	32 (27, 5)
Total	50,137	57		32	150 (96, 54)

Table 2.
Comparison of Productivity of Cases by 4 Different Approaches

	No. of person examined	T. B. Suspect	Open case
Before mobile X-ray clinic	—	—	57
1st mobile X-ray clinic	226	72	3
2nd mobile X-ray clinic	1,022	191	32
3rd mobile X-ray clinic	24,641	952	150

Before the mobile X-ray clinic started, the registered open cases are only 57 which were found by the routine sputum examination in the local health stations or transfered from the T.B. clinics.

226 symptom motivated cases attended the first mobile x-ray clinic, 1,022 symptom motivated cases attended the second mobile X-ray clinic and 24,641 persons (79.7% of the age group of 10 and over) attended the third mobile X-ray clinic. 72 suspicious cases including 3 open cases in the first mobile X-ray clinic, 191 suspicious cases including 32 open cases and 952 suspicious cases including 150 open cases were found in the third mobile X-ray clinic. Culture of the sputum were done to those suspicious cases. The different results of the case-fihding were due to the different approaches in the community:

1) Before May 1978: Only direct sputum smear examinations were used.

2) 1st mobile X-ray clinic: Only one official paper to ask the local health station to gather the symptom motivated cases to attend.

3) 2nd mobile X-ray clinic: Three times of discussion with the local health stations before the official paper issued.

4) 3rd mobile X-ray clinic: Organize the whole community step by step by asking the whole population to attend.

23. Case-finding in Japan, its Efficiency

Dr. S. Sakamoto, Japan

According to the TB Control Law, the annual TB examinations are to be made in the whole population of the country, infants to be subjected by tuberculin skin test, and the remaining (over 5 years of age) to be X-rayed as well.

The primary case-finding is usually carried out by 35mm, 60mm or 70mm radio-photography subjecting all adults and all tuberculin reactors in children. Those found with abnormality by radiophotography are subjected to bacteriological examinations, both microscopy and culture.

A total of about $ 7.4 million is spent yearly for the examination of about 43 million persons, to detect about 62,000 TB suspects. Namely the sum of ¢ 17 is spent per examinee and the cost per one TB suspect detected is $ 120.

As can be estimated from the above, only 40% or so of the total population is covered by the annual examination, in spite of efforts and costs paid in the country.

The results of the above-mentioned activities are rather surprisingly low, namely only 51.7% of bacteriologically positive cases have been detected, according to the 1968 country-wide sample survey of the country. On the other hand, it was known by the same survey that 41.7% of bacillary cases were symptomatic. This means that, should examinations of any effective kind be applied concentrating

in those, who have chest symptoms, 41.7/51.7=80.7% of existing cases would be detected.

In fact, in various areas in Japan, the efficiency of the mass case-finding by the present method is being assessed to be found surprisingly poor. For example, only about 30% of newly registered TB patients were those detected by the mass examination, and the remaining majority were by clinics and hospitals on their voluntary visits with symptoms.

Now, there are studies and trials being carried out to find more efficient case-finding methods taking the above in consideration

24. Case-finding in Singapore

Dr. Wong Hin Sun., Singapore

The primary casefinding measure in Singapore is based on chest x-ray followed by full bacteriological examination and clinical examination of all cases showing lung abnormalities in the Chest X-ray. Chest X-ray examination is offered to the community as in table attached. Cases of tuberculosis discovered are notified compulsorily by law to the Central Tuberculosis Registry where accurate statistics are kept and published annually. In the last few years the proportion of cases notified was approximately 75% from Government agencies, 20% from the Anti-tuberculosis Association, 2% from general practitioners and 3% from notifications after death.

Casefinding by Mass X-ray of the Community above the age of 15 years had a total coverage that varied from 46% to 88% giving an average coverage of 55%. The

yield of active pulmonary tuberculosis for all the areas covered was 23.5 per 1,000 X-rayed out of which 7.1 per thousand X-rayed were bacteriologically positive.

Examination of Contacts of Tuberculosis Cases yielded 23.0 active cases per 1,000 examined and 15 inactive cases per 1,000.

Investigation into 8,971 symptomatics in the out-patient dispensaries between August to December 1969 produced 12.1 active pulmonary tuberculosis cases per 1,000 examined out of which 8.1/1,000 were bacteriologically positive. The yield from examination of statuatory groups like school staff, school leavers and national servicemen remained low.

In 1969 a detail study was made on all cases registered for treatment in the treatment institutions in Singapore to asses the relative merits of Direct Smears and Culture examination as a casefinding measure in an institution where the laboratory facilities is of a relatively high standard. A total of 1,162 cases was taken into the study. Two specimens of sputum were collected from each patient and subjected to examination by direct smear by florescent microscopy and then cultured.

1. The findings showed that initial smear examination of all the patients and subsequent smear examination of a second specimen of sputum in those found negative on first examination yielded 500 positive cases.

2. Culture examination of the first specimen yield a total of 582 positives.

3. Initial smear examination of all patients and smear examination of a second specimen in those initially smear negative *plus* culture examination of the initial specimen would yield 636 positive cases.

4. Smear and culture examination routinely in both specimens in all patients detected 705 positive cases.

Taking the cost of direct smear examination as unity, the relative cost of routine smear plus oulture on a single specimen from all patients is 4.5. The cost of examining a specimen by culture only in patients smear-negative on examination of two specimens is 3.5 and the routine culture and smear examination of two specimens in all patients cost 9.1.

25. Case-finding Program in Taiwan

Dr. S. W. Luan, Republic of China

There are three ways of case-finding in Taiwan. One is by community-wide mass chest X-ray survey with 70mm miniature film. The other way is selective mass chest survey by mobile X-ray clinic. The third way is direct microscopic sputum examination.

I. Community-wide Mass Chest Survey with 70mm minature film followed by sputum examination (or laryngeal swab) for the X-ray positive cases has been carried out in the last seven years. All adults above 20 years of age were eligible for examination. The response was fairly well in 1963 (86.3%) and cooling down in 1969 (58.5%).

The case yeilding for TB suspects is 4.4%, for infectious case is 0.7%. For the last seven years, a total of 1,377,420 people has been examined by 13 mobile 70mm X-ray units. The total population in Taiwan is around 13 millions now, it is obviossly impossible to cover the whole island in the coming 10 years.

II. Selective Mass Chest Survey by mobile X-ray clinic —a modified method. In this method, mobile X-ray units was sent to the rural area twice a year to X-ray those with respiratory symptoms. Then followed by sputum examination for those with X-ray shadows. From 1966-1969, 143,693 people has been examined. Case yeilding for TB Suspects is 12%, for infectious cases is 2.5%. Four times more than that of community-wide survey.

III. Direct Mircoscopic Examination. This method was started from 1963. In the begining, the work was done mainly by laboratory technicians of the Health Stations. Since October 1966, another 200 high school graduated girls were recruited to take their place.

In order to evaluate which method is superior, the work done in Chiayi in 1968-1969 were reviewed and analysed. It is easily to realize that selective MCS is mach superior than community-wide MCS in terms of both discovery rate and operational cost. The discovery rate of selective MCS is 9.8% for TB suspects and 2.7% for infectious cases. While in community-wide MCS, it is only 4.1% and 0.4% respectively, about one half to one-seventh of that of selective MCS. Furthermore, selective MCS discovers more infectious cases (27.3% versus 8.5%), especially among minimal and moderately advanced (without cavitation) cases. It is because that symptom motivated examinees suffer more active and progressive lesions than that of routine chest exmminees. Case yeilding of mass sputum survey (direct microscopic sputum examination) is rather poor. This work which had been carried out in Chiayi Region in the year 1968 by 43 newly recruited "TB Workers" was also reviewed and analysed. They are asked to visit people above 45 years of age house by house to collect sputa for examination. Only 202 infectious cases discovered among 16,150 people with 16,901 specimens examined in a whole year

by these 43 TB workers. Among 202 infectious cases, 81 (40.1%) are far advenced with cavitation.

As to operational cost, it costs only NT$469.0 (or US$ 11.7) to discover one infectious cases by selective MCS but NT$3117.0 (US$77.9) by community-wide MCS and NT$ 1415.0 (US$35.4) by mass sputum survey-direct microscopic sputum examination.

In conclusion, selective MCS is very effective in case-finding both in terms of efficiency and operational cost. It is hoped to discover all infectious cases within reasonable period of short time, say three years by means of selective MCS in this country.

26. An Evaluation of the Reliability and Efficiency of Sputum Smear Examination in Case Finding of Pulmonary Tuberculosis

Dr. Chi-Chung Lin, Republic of China

Sputum smear examination is the most reliable and convenient method for case finding of pulmonary tuberculosis. The method will not be of any use, however, if the positivity is too low and/or if the examiners make a wrong report. In an attempt to evaluate the present status a comparison was made on the result of the sputum tubercle bacilli examinations performed by public health workers, laboratory technicians and bacteriologist.

Method: Tubercle bacilli, measuring 1 mg (10^9), were poured into an 100 cc. admixture containing 50 cc egg-white and another 50 cc glycerin. The mixture was diluted 10 to 100 times for making smear slides with

the suspension having tubercle bacilli measuring 10^7, 10^6 and 10^5 in each cubic centimeter. Another slide was prepared with an egg-white glycerin solution without containing the tubercle bacilli. All slides were treated with Ziehl-Nelsen stain. With four slides a set, they were distributed to 98 public health workers who had received a course of three day training of sputum TBB examination and who were engaging in tuberculosis case finding at rural health stations. Meanwhile 19 laboratory technicians who were working at Tuberculosis Control Center, were also asked to participate in the experiment. All of the participators were requested to hand in the results of their examination within a day.

As shown in Table 1, out of 98 public health workers these were only 20 (20.4%) who obtained correct answers for all of the four slides. Surprisingly, as many as 35 (35.7%) workers made one misjudgment. The number of those who made two mistakes came up to 22 (22.4%), three mistakes 17 (17.4%) and four mistakes, i. e. all mistakes 4 (4.2%). On the other hand, 8 (42.1%) out of the 19 technicians got correct answers for all of a set of four slides. For the rest of 11 persons, 7 (36.8%) made one mistake respectively, 3 (15.7%) two mistakes and 1 (5.2%) three mistakes. The laboratory technicians seemed to have obtained better results than the public health workers though all of the results were not at all satisfactory.

The wrong reports investigated according to the number of bacilli were shown in Table 2. The examiners were liable to make misjudgment when the number of bacilli was as small as 10^5 while 68.5% of those who made one mistake came within the category. For those who made more than two mistakes, the number of bacilli seemed to have no concern with the misjudgment. There were 8 (8.1%)

public health workers and 2 (10.5%) technicians who made false positive report, i. e., reporting negative ones as positive. To prevent erroneous reports and for impovement of sputum examinations reinvestigation of laboratory technique is recommended.

In Table 3 was the result of one sputum examination made by a bacteriologist, who was working at Taipei Tuberculosis Control Bureau. He did not make a false positive report after examining the sputum from 366 cases with normal chest x-ray His result of positive finding was as follows:

Table 3. Correlation of X-ray and Becteriological Findings of 443 Persons

Taipei Tuberculosis Control Bureau

X-ray diagnosis	Result of Smear Exam.		
	Positive(%)	Negative	Total
Normal	0	366	366
Minimal	2 (7.4)	25	27
Mod. advanced s cavity	3 (17.2)	15	18
Mod. advanced c cavity	8 (72.7)	3	11
Far advenced s cavity	2 (66.7)	1	3
Far advanced c cavity	13 (72.2)	5	18
Total	28 (36.4)	415	443

Likewise, the results obtained by the technicians of the N.T.U.H. were listed in Table 4. The positive rates were as follows:

Table 4. Correlation of X-ray and Bacteriological Findings of 115 Persons (N.T.U.H.)

(National Taiwan University Hospital)

X-ray Diagnosis	Result of Smear Exam.		
	Positive(%)	Negative	Total
Minimal	1 (3.3)	29	30
Mod. advanceds cavity	2 (10.5)	17	19
Mod. advanced c cavity	9 (37.5)	15	24
Far advanced s cavity	9 (34.6)	17	26
Far advanced c cavity	6 (37.5)	10	16
Total	27 (23.5)	88	115

As can be seen from the above data, there is a significant difference between the results of public health workers and those of laboratory technicians. Still more noteworthy is the difference between the results brought forth by the bacteriologist of Taipei Tuberculosis Control Bureau and the technicians of the N.T.U.H It is assumable that the positive rates may show a great difference when the examinations are made at different environuents. Needless to say, the sputum TBB detection must be checked constantly when applying the examination in case-finding of pulmonary tuberculosis. Re-training is recommended for those who bring forth low positive detection rates.

27. Case-finding in Thailand

Dr. Boousong Sunakorn, Thailnd

Since 1951, the Division extended its services by increasing the number of TB centers, to strengthen the country-wide tuberculosis control programme by completing the system of Zonal TB centers under the existing Regional

TB control centers. Each of the Zonal TB centers will be responsible for the control of tuberculosis in an area with the population of about two million. The main function of the Regional and Zonal TB centers will be gradual implementation of the National Tuberculesis Centrol Programme throughout the country. Since the bulk of tuberculosis problem is located in the rural areas, 85% of the population live in the villages particular attention will be focused on tuberculosis control in the rural part of the country. The only possible way to fulfil this plan is to adopt and accept the simplified case-finding method, viz. sputum smear examination of symptomatic persons. Since 1966, a total of about 70 TB workers were stationed in at least one each in the first class health center of each province of the whole country, averagely 44 cases were detected in 300 symptomatic persons smear-examine per worker per year. However, most of the peripheral centers without TB workers stationed were beyond the reach of the TB workers to let them follow or cooperate with the programme. There are altogether about 250 first class health centers in the whole country, if all of them are utilised fully in the diagnosis and treatment of tuberculosis and also establishing co-operations between the National TB Programme with all the existing facillities i. e. Provincial and District general hospitals and the diagnostic laboratories, the tuberculosis control programme will be mostly effective.

28 BCG Vaccination by Multiple Puncture Method Employed in Japan

Dr. Tetsuji Sawada, Japan

The intradermal vaccination used to be not quite popular due to some possible cases of severe local lesions such as

ulcer and keloid-formation particularly in girls from cosmetic point of view.

Many ways of percutaneous vaccination had proved that the local lesion was slighter than in the intradermal vacoination, while the tuberculin reaction induced was weaker than in the intradermal vacoination.

The multiple puncture method by using the new apparatus provided with nine thin needles proved that the tuberculin reaction induced was comparable with that in the intradermal vaccination and the local lesion was much slighter than in the intradermal method.

The further study proved that the tuberculin reaction and local lesion induced after vaccination related to the pressure of the apparatus on the skin and the viability of vaccine.

29. Comparison of Multipuncture and Intradermal Methods in the Post-vaccination Tuberculin Allergy Level

Dr. Y. Azuma, Japan

The study was made on an occasion of BCG scar study in co-operation with Dr. Boonsong Sunakorn of the Tuberculosis Control Division, Thailand, in 1967. A total of 180 children of 4-9 years of a kindergarten and a school were subjected to the study. All the subjects are those who showed a tuberculin reaction of 0-9mm induration size at the initial tuberculin test with 2 TU of PPD-S RT 23 with Tween 80.

The BCG vaccination was given by multipuncture and intradermal methods, allocated rotationally to the children. The number of children is not the same between the two

groups although the methods were allocated strictly rotationally, as the vaccination was given on the same day of tuberculin test without waiting for reactions to be read. Those vaccinated by multipuncture method were numbered on their individual cards with the serial order of the vaccination within ampoule.

Table 1 gives the distribution, and the mean size as well, of tuberculin reactions by induration size at two months after the vaccination in both groups. The results were poorer with the multipuncture method than with the standard so far as judged by the post-vaccination tuberculin allergy level. However, as shown by the last three columns of the table, the mean size was quite comparable when only those were considered who were vaccinated by multipuncture using earlier vaccine drops from each ampoule. The mean size was 14.2mm in the first 12 children of each ampoule, but decreased in the second 12 to 11.6mm and in the third 12 to 10.0mm.

The vaccines were reconstituted at the working site, under roof at a room temperature of about 30°C, immediately before use, allowing not more than one ampoule opened at the same time in each method. An ampoule of vaccine was used within 30 minutes after reconstitution.

The above results show that the post-vaccination tuberculin allergy level is less constant with the multipuncture method compared with the standard intradermal method. Should the number of children to be vaccinated be limited within twelve or so per ampoule, the former method would give results comparable with the standard method.

The multipuncture method is attractive from cosmetic view-point, leaving almost unnoticeable scars in most cases after 1-2 years of vaccination, but its weak point is the difficulty in controling the vaccination dose.

Table 1. The distribution of tuberculin reactions by size in children with initial tuberculin reactions of 0-9mm size at two months after BCG vaccination by intradermal and multipuncture method.

Post-vaccination tuberculin induration size	Intradermal	Multipuncture			
		Total	Serial numbers* within ampoule		
			1—12	13—24	25—36
0—1mm	2	6	1	1	4
2—3	3	6	•	4	2
4—5	•	1	•	1	•
6—7	1	•	•	•	•
8—9	•	3	•	1	2
10—11	3	9	2	6	1
12—13	12	13	5	4	4
14—15	29	19	11	6	2
16—17	30	23	11	7	5
18—19	15	4	2	1	1
20+	1	•	•	•	•
Total	96	84	32	31	21
Mean size	14.7mm	12.2mm	14.2mm	11.6mm	10.0mm

Vaccines used:

for multipuncture method: Japanese freeze-dried BCG vaccine, Lot No. K-1, 054-F, reconstituted at a concentration of 80mg/ml.

for intradermal method: Japanese freeze-dried BCG vaccine, Lot No. 11-129-E August 1966, reconstituted at a concentration of 0.5mg/ml.

*) The post-vaccination tuberculin reactions in this group are tabulated by the serial number by which the vaccination was given within ampoule.

30. Studies on Post-vaccination Reactions in Schoolchildren Vaccinated with Liquid and Freeze-dried BCG Vaccines

Dr. W. C. Chow Republic of China

In view of operational advantages more widely use of freeze-dried BCG vaccine had been recommended by the second Symposium on BCG Vaccine Production in the South-East Asia and Western Pacific Regions, WHO, which was held in Manila, Philippines on September 1969. BCG vaccination has been one of the most important measures in TB control program of Taiwan. In past 20 years most of vaccines used in the field were local produced liquid BCG vaccine, only a small number of freeze-dried vaccine has been imported for use in some remote area where the transportation and storage of liquid vaccine are not available.

Great efforts have been made in the laboratory to produce a vaccine of fairly uniformity and high potency for use in the BCG program. Yet, fluctuation are heard from time to time which mainly caused by decreasing of potency of the vaccine during transportation and unproper storage. Furthermore, quite a big amount of liquid BCG vaccine has been wasted because of their short expiry peroid. For example, in 1969, about 4 million doses of liquid BCG vaccine were produced by the BCG Laboratory, and the vaccination numbers of the same year were about 900,000, only one fourth of vaccine produced had been administrated to the vaccinnees.

In considering the estimated costs for producing freeze-dried BCG vaccine and comparing with the operational advantages, it is decided to try to explore the feasibility for the laboratory to produce locally the freeze-dried vaccine for field use.

A comparative study on potencies of liquid and freeze-dried vaccine were designed to screen the post-vaccination reactions of the two vaccines in March 1970 in Taiwan.

Approximately 600 first grade primary school-children without old BCG vaccination scar who don't show positive reaction to tuberculin (i. e. whose induration size is below 10 mm) were examinees for the studies. Two freeze-dried (Japan & Denmark) and one liquid (Taiwan) BCG vaccine were used in the studies, about 200 school-children were vaccinated with each vaccine. The results of post-vaccination tuberculin sensitivity and vaccination lesion will be measured at 3 and 12 months in the first year, and 2, 3, 4 and 5 years after vaccination. The results at the 3rd month have shown that the mean induration size was 14.0 mm for the Japanese freeze-dried vaccine, 11.2 mm for the Danish freeze-dried vaccine and 13.9 mm for Taiwan liquid vaccine. The potency of Taiwan produced Liquid vaccine was identical to Japanese freeze-dried vaccine.

31. Epidemiological Study of Abnormal BCG Scars Among School Children

Miss H. C. Chu, Republic of China

Many BCG keloids have been encountered by the physicians in last several years and Hsing warned that the resulting keloid formation, as high as 10% by his study, will endanger the prestige of BCG vaccination in the future.

In order to obtain more informations on the prevalence of BCG keloid and, if possible, the cause of it, an epidemiological survey was made among pupils at the third and fifth grade of primary school and eighth and eleventh grade of high school in the northern part of Taiwan.

A class was used as a sampling unit and 44 out of the total of 1,390 classes of the third grade and 45 out of the total of 1,353 classes of the fifth grade were selected randomly. For the high schools 74 out of the total of 701 classes of the eighth grade and 63 out of the total of 321 classes of the eleventh grade were selected. A total of 12,313 pupils were examined, 6226 being males and 6087 females.

Diagnostic criteria used in this survey for the term of "abnormal BCG scars" are:

1 Keloid:

An elevated hard or elastic firm mass which has at least one of the following characteristics.

(1) Having projections like crab claw
(2) Larger than the original scar
(3) Telangiectasis and tense red margin
(4) Still growing
(5) Itchy or painful sensation

2. Hypertrophic scar

An elevated hard or elastic firm mass which has none of the above mentioned characteristics.

3. Atrophic scar

A scar which is depressed from the normal skin and in which the skin appendages have disappeared.

The overall rate of children with abnormal BCG scars was 28.0%; in which 4.7% with keloids, 22.2% with hypertrophic scars and 1.1% with hypotrophic scars. The frequency of keloids increased with age from 1.6% at third grade to 3.4% at the fifth grade and 6.7% at the eleventh grade. It was more frequent among female than male, 8.0% as compared with 5.2% at the latter grade.

Higher prevalence of abnormal scars was observed among the children with more than one BCG scar.

Considering the size of the abnormal scar 90% of the scars were smaller than 10 mm for the primary school children and 70% for the high school children. Bigger scars over 20 mm were extremely rare among children under 12 years of age and 2.4% among high school children.

The definition for a "normal scar" and "abnormal scar", or a scar is acceptable cosmatically and a scar is unacceptable cosmatically (ugly) is not clear, and further more the criteria used for "Keloid" are confusing again on several reports.

One fact is centain that there is a problem of BCG scar which concerns the vaccinated children and their parents as well as the public health officers. Athough the problem is not serious, ways and means to prevent the creation of such a problem should be investigated and endeavoured by all of us.

32. The BCG Vaccination Programme in Japan

Dr. Y. Azuma, Japan

The BCG vaccination is compulsory in Japan. Since 1948, all the population is to be subjected to the annual TB examination and those below 30 years of age are to be screened by tuberculin skin test for BCG vaccination. Old Tuberculin for the skin test was replaced by a Japanese PPD in 1968, and a multipuncture method was adopted for the vaccination in 1967.

About $200,000-360,000 was annually spent on the BCG programme since 1951, its proportion in the Governmental

TB budget varying between 0.2 and 4.8%. A total of 169 million yen (about $ 470,000) was spent for the programme, 0.44% of the total TB budget, 38,330 million yen ($106.5 million) in 1968.

The coverage of BCG vaccination has been improving since it began to be applied widely in the country in 1942, and particularly since 1948. The overall coverage in the population was 53% in 1968. However, the coverage is not high enough in infants. It was 43.2% in infants below 5 years, while over 80% in older children in the country-wide sample survey, 1968. An intensification of the primary vaccination activities in young infants by reducing the re-vaccinations is under consideration, studies being made on the subject.

Studies were made on the protective effect of BCG vaccination in man by several research workers, their results being summarized in the Report by the BCG Research Committee of the Japan Society for Promotion of Sciences, 1943, opening the BCG epoch in the country's TB control programme. The tuberculosis incidence and death rate were compared between vaccinated and unvaccinated groups in the studies, however, the observation time was mostly not over 5 years.

There have been few control studies on the protective effect of BCG carried out since then, due to the compulsary vaccination in the country.

The tuberculosis incidence has been decreasing with the increasing proportion of the vaccinated in the whole population In the one-year follow-up studies of sample populations made in 1953/54, 58/59 and 63/64, it was observed that the older generations were being replaced gradually by the younger generations with higher BCG coverages, resulting a higher overall coverage, and that the annual

TB incidence was decreasing with the increase of the coverage. The overall BCG coverage, adjusted to the age distribution of 1963/64 sample population, was respectively 42.1%, 43.0% and 53.0% in 53/54, 58/59 and 63/64, and the adjusted annual incidence 3.6%, 2.0% and 1.6% correspondingly.

There is hardly a problem of complications of BCG vaccination in Japan, since the present method has been found very good from the cosmetic point of view, BCG scars by the method becoming almost unnoticeable in a couple of years in most cases. However, the method has a weak point, which is the difficulty in the vaccine dose control, though a post-vaccination tuberculin sensitivity level, comparable to that by the intradormal method, can be obtained by limiting the number of vaccinations per vaccine ampoule.

Table 1. The BCG coverage by age in Japan
—by the 1968 country-wide sample survey

Age	BCG coverage %	Age	BCG coverage %
0—4	43.2	45—49	18.8
5—9	80.3	50—54	12.7
10—14	82.3	55—59	8.5
15—19	78.9	60—64	5.3
20—24	78.1	65—69	3.6
25—29	78.5	70—74	2.0
30—34	72.2	75—79	1.5
35—39	55.5	?	26.7
		All ages	53.0

Table. 2. The trend of Governmental tuberculosis budget

Fiscal year	Governmental Tuberculosis Budget in Million Yen			Remarks
	Total	BCG vaccination incl. skin test	ditto, % against the total	
1949	186	8	4.30%	* Freeze-dried BCG adopted, 1949/50.
1951	2,747	91	3.31	** Criterion for the free hospitalization up-raised.
1953	2,643	84	3.18	*** The fund for TB treatment largely increased to enable a wider application of secondary drugs.
1955	2,133	102*	4.78	****Multipuncture adopted.
1957	2,937	131	4.46	
1959	3,341	84	2.51	
1961	17,029**	98	0.58	
1963	27,859***	77	0.28	
1965	37,956***	79	0.21	
1968	38,330	169****	0.44	

Table 3. The BCG coverage and the TB incidence in sample populations of the follow-up surveys, 1953/54, 58/59 and 63/64

		Age groups					All ages	All ages adjusted to 1964*
		0—14	15—29	30—44	45—59	60+		
SAMPLE POPULATION SIZE	53/54	5557	3297	2536	1728	1129	14247	
	58/59	6687	4633	3645	2580	1752	19297	
	63/64	6269	4779	4271	3025	1998	20342	
BCG COVERAGE IN %	53/54	73.4	58.5	18.3	8.7	6.1	47.4	42.1
	58/59	69.9	66.7	20.3	7.8	3.8	45.5	43.0
	63/64	77.9	77.4	40.5	13.6	4.9	53.0	53.0
TUBER-CULOSIS INCIDENCE PER 1,000	53/54	4.3	3.3	5.5	1.7	0.9	3.7	3.6
	58/59	0.3	2.2	3.3	3.5	1.7	1.9	2.0
	63/64	0.6	1.0	2.6	1.7	3.5	1.6	1.6

*) As the age distribution of the sample population varied between the three follow-up studies, the overall BCG coverage and TB incidence were calculated by adjusting them to the age distribution of 1964 sample population.

33. The BCG Program in Taiwan

Dr. C. W. Chao, Republic of China

1. General

Tuberculosis Control program in Taiwan was actually started with BCG program. In the late 1940's under the conditions prevaling in Taiwan the only measure which could be quickly organized was BCG vaccination of uninfected individuals, because of its cheapness and easy administration.

The main feature in the organization of the BCG program has been that it is totally integrated into the general public health services. In Taiwan, this means the participation of the 22 health bureaux and 365 health stations.

The second feature of the BCG program is that it is carried out by the regular health workers in the foregoing health agencies without employing additional workers.

In the early phase of the program the vaccination was largely given to the school children population mainly by the 22 health bureaux and 4 TB centers. After a successful study in 1962 on the simultaneous administration of BCG and smallpox vaccination, training of health station workers was begun in 1963 and by the end of 1965 all the 365 health station workers have been able to perform BCG vaccination. This is really a break-through in tuberculosis control in Taiwan for not only has the total number of vaccinations greatly increased, but the problem of vaccination at a critical age has changed a lot with the preschool children and especially infants greatly boosted in proportion.

At the end of 1969, a total of 11.3 millons of BCG

vaccination were given.

2. Direct BCG vaccination

The result of the 2nd tuberculosis prevalence survey conducted in 1962 indicated that the infection rate (tuberculin positive reactors) among the infants under one year of age was only 0.3%. This finding initiated the idea of elimination of tuberculin testing as a routine measure prior to BCG vaccination. Two observations were made subsequently on giving the BCG vaccination to the tuberculin reactors among the children aged between 5-14 years. No serious untoward effects were observed with the exception of accelerated and severe local reactions, the "koch's phenomenon".

Direct vaccination for the infants by simultaneous BCG and smallpox was thus launched province-wide since 1965.

3. Coverage

It is reported that during the last 4 years about 80% of the eligible infants born during each year was covered with BCG vaccination.

In the rural areas, at present, during community tuberculosis campaign direct BCG vaccination has been applied to the children under 5 years of age.

Observations on the prevalence rate of BCG vaccination scars were made during the second and third tuberculosis prevalence surveys. It was found that 23.8% of the population 10 years and over in 1962 and 34.2% in 1967 have at least one BCG scar, and a considerable increase in the prevalence rate of BCG vaccination scars for all age groups from 10-29 years during the five years period.

The prevalence rate of BCG vaccination scar among children below 5 years of age was 7.1% in 1957, 7.4% in 1962 and increased to 46.3% in 1967. The high prevalence rate of scar among children in 1967 was apparently due to the general application of simultaneous smallpox and BCG vaccination since 1965.

4. Effectiveness

Taiwan has been one of the few countries that endeavours to maintain an organized mass BCG program for as long as 20 years. Considering the operational technique and costs, the program has been remarkably efficient. Nevertheless, it was unfortunate that a controlled population was not planned in order to evaluate the effectiveness of the BCG program in a more precise way.

However, supportive data are avilable to indicate that BCG vaccination is effective for the reduction of the tuberculosis rate.

Firstly there has been a continuous and remarkable decrease in tuberculosis rates among the younger population, especially under 30 years of age, which was about 1%, while the rate for the population 45 years and above was 5-6 times higher in 1967. Since the BCG vaccination program started as early as in 1950, when school children were the main objectives, the present population under 30 years have been largely protected.

The second information on the effectiveness of the BCG program in Taiwan was obtained from a retrospective observation during the third tuberculosis survey in 1967 on the prevalence rates between the population groups with and without BCG scar below 30 years of age. It has been estimated that BCG vaccination prevented approximately 50-60% of tuberculosis incidence in Taiwan.

5. Operation and techniques

a. The vaccines:

Liquid BCG vaccine produced in the BCG Laboratory of the Taiwan Serum and Vaccine Laboratory is in use except in some remote areas where Japanese freeze-dried vaccine is in use. The strain of BCG in Taiwan is from the Pasteu Institue in Paris. The vaccine is made in two different concentrations; one contains 1 mg of BCG per ml. and the other contains 0.5 mg of BCG per ml. the former is given to school children and preschool children while the later is given to infants and new-borns.

b. The Method:

1 Tuberculin Unit of PPD RT23 with tween 80 is used for the children who require pre-vaccination tuberculin testing. The result is read 72 hours after the testing and an induration with transverse diameter smaller than 10 mm is regarded as negative reators and BCG vaccination is given. 0.1 ml. of the vaccine in either concentration is given intradermally to the upper deltoid region of the left arm.

c. Delivery of vaccine

The BCG Laboratory dispatches fresh BCG vaccine on fixed days of the week upon the request from the health bureaux. The vaccines ampules are packed in a specially designed icebox and sent to the destinaion (health bureaux) by railway transportation. The vaccines can be reached to all health bureaux within 24 hours and there be kept in refrigerator. The health stations collected the vaccines from health bureaux whenever they are in need. The vaccinators carry their vaccine in a plastic ice-container during the

actual inoculation in the field. BCG vaccines stored beyond two weeks are to be discarded.

d. The duties

The simultaneous vaccinations are given to infants by health station personnel twice a year in Spring and Autum, while the vaccination of school children are still mostly by county/city health bureau nurses. The vaccination of preschool children are done by nurses of the Tuberculosis Control Centers or the health bureaux or by the health stations personnel and the vaccination of new-borns babies are made by nurses in hospitals.

e. The cost:

It has been roughly estimated that the operational cost per vaccination was around NT$2.0 (US$0.05) and the proportion of the fund used in BCG vaccination program is around 10% of the total funds spent for tuberculosis control program in Taiwan.

We believe, if we are to endeavor this BCG program for another 20-30 years when majority (90%) of the population will be protected by BCG, the tuberculosis situation can be reached the stage when it will not constitute a hazard to public health in Taiwan.

34. BCG Vaccination in Hong Kong

Sister M. Aquinas, Hongkong

BCG coverage of at least 80% of a susceptible population is an undisputed recommendation in a region with a high transmission rate of tuberculosis.

For almost 20 years Hong Kong has been using BCG on a large scale and in recent years about 95% of newborns have been receiving this vaccination. The geographical and physical conditions of the area facilitate the extensive application of such a procedure but the qualitative aspects of the programme are less easily calculated.

The paper discusses some of the difficulties that arise in allocating precise merits to the BCG campaign in the subsequent decline of tuberculosis, especially when other control measures are in opera tion at the same time.

35. Assesment of BCG Vaccine and of the BCG Vaccination Campaign in Taiwan

Dr. W. C. Chou, Republic of China

1. Purpose

In order to check whether the operational and technical performance of a BCG vaccination programme is being maintained at the highest possible level, if it is not, to identify the reasons for any shortcomings in this respect, regular evaluations are made of the potency of the vaccine used in the campaign so that, if unsatisfactory results are revealed by the assessment, steps can be taken to correct the faults and bring the campaign up to standard again.

2. Training

In November 1968 a training course on BCG assessment was held in the Taiwan Provincil Tuberculosis Control Bureau, with the assistance of Miss E. Wilhelmsson, WHO Regional Standard tuberculin reaction reader. Seven nurses

well-experienced in tuberculin testing and BCG vaccination participated in the course from the four Tuberculosis Control Centers in Taipei, Taichung, Chiayi and Tainan.

3. Method

The province-wide assessment on simultaneous smallpox and BCG vaccination given to infants by health station personnel was conducted during the spring and autum campaign in 1969.

The assessment was made in two main parts, namely; the assessment of the potency of BCG vaccine by means of viability count and the assessment of the post-vaccination tuberculin sensitivity and vaccination lesions 9-12 weeks after vaccination.

A) Assessment of the potency of BCG vaccine

a. BCG vaccine produced and stored at BCG laboratory

Viable units were counted on sample ampules of every batch in the first and third weeks of production at the BCG laboratory. Post-vaccination tuberculin sensitivity and vaccination lesions were measured among approximately 300 primary school children who have no BCG scar and showed negative tuberculin reactions.

b. BCG vaccine being used in the field

The vaccine in ampules opened during BCG vaccination of infants by health station personnel were collected by assigned nurses and sent directly to BCG laboratory for viability count. Twenty health stations in the province were selected for the assessment by random sampling method with stratification by Tuberculosis Control Center Regions.

B) Assessment of BCG vaccination

The BCG vaccination given to infants by health stations personnel was assessed by measuring post-vaccination tuberculin sensitivity and vaccination lesions 9-12 weeks after the vaccination. The sample health stations for the vaccintion assessment were the same as those for the vaccine assessment.

4. Results

The BCG vaccine produced in the BCG Laboratory in Taiwan, showed strong viability when it is inoculated within one week after production. The viable units of the vaccine containing one mg of BCG per ml. (dose for children over one year of age) had the mean at 37.4×16^6 and those of the vaccine dilution containing 0.5mg per ml. (dose for infants below one year of age) had the mean at 39.8×10^6.

The potency of the vaccine as expressed by the post-vaccination tuberculin sensitivity is also satisfactory. The mean induration size of the post-vaccination tuberculin reaction was 13.7 mm and the mean vaccination leasion size was 5.1mm. on primary school-chidren.

The viability of BCG vaccine dropped considerably within two weeks from the first to the third week after production while it was kept in the BCG Laboratory, Taipei.

Half of the vaccine collected during the vaccination of infants in twenty sample health stations showed more than 10×10^6 viable units and the remaining half showed less than 10×10^6 viable units and were aged 10 days or more.

The mean induration size of post-vaccination tuberculin reactions among infants by the personnel of twenty health stations ranged 5.0mm to 11.6mm at 8-15 weeks

after vaccination.

The mean vaccination lesion size ranged 3.3mm to 6.9mm.

5. Improvements

The results of the BCG assessment during the spring campaign in 1969 has been used for corrections and improvements in the quality control of BCG vaccination program in Taiwan.

36. BCG Vaccination Programme in Thailand

Dr. Boonsong Sunakorn, Thailand

This preventive aspect of tuberculosis control has been practised in far wider scale since the beginning of the control programme in 1953. A total of 5,635,789 vaccinations was made during 1954/1965 by the specialised mobile BCG teams, of these 29% in the age group 0-6 years and 55% in 7-14. The work load averaged at 469,649 vaccinations a year (not included the number of pre-tuberculin tested), which is less than the annual population increase. A utilization of existing facilities of the general health services was needed to catch up with the population increase and also to cover more of the younger generation. This could be done only after a simplification of vaccination method was adopted facilitating the training of provincial health staff after a successful trial of direct BCG vaccination in 1965. The BCG vaccination programme was integrated in the general services since 1967. The transportation and storage of vaccine became much easier when the heat-stable glutamate freeze-dried BCG vaccine was used, except in Bangkok and near-by provinces, where Thai liquid vaccine

were available without difficulties. During this integrating period, 1967-1969, a total of 5,368,349 vaccinations was performed with the average of about 1,780,000 vaccinations per year. This was considered to be a very great improvement.

Concerning about the efficiency of BCG vaccine, it is expected that the result will not be very much less than that observed by the British Medical Research Council. Though no such study has ever been made in this country, there are some data suggestive of the above. Namely, it was found in the entrance examination of the students applying for the universities in Bangkok during the last three years, that the prevalence of tuberculosis suspects and cases was lower by about 70% in those who had been BCG vaccinated before than in those un-vaccinated. The other indirect evidence is that the lowering of the yearly incidence of milliary tuberculosis as well as tuberculous meningitis.

37. KAP Survey on Tuberculosis

Dr. Nak Chin Chung, Republic of Korea

38. Changes in Prevalence & Incidence of Pulmonary Tuberculosis in Recent Years

Dr. S. P. Pamra, India

The New Delhi Tuberculosis Centre has a population of about 30,000 under surveillance in the city of Delhi since 1962 with a view to study the epidemiology and the

time trends of pulmonary tuberculosis in an urban population. Since 1962, this population has been surveyed four times at intervals of 2½ years each. The coverage each time has been over 90% of the eligible population. Children under 5 years have been excluded. 70 mm film has been taken for all those available. Films have been read by two independent readers and those persons whose miniature film was marked abnormal by either or both the readers were called to the Centre for further investigations. These investigations consisted of sputum/laryngeal swab examination by direct smear and culture and conventional size film, if necessary. Aetiology and activity of the lesion were established, if necessary, after a period of observation extending in some cases up to 6 months during which at least two sputum/laryngeal swab cultures and radiological examinations were carried out.

The last survey of the series was completed in January, 1970. Data on the following will be presented:-

1. Prevalence of disease, bacillary as well as abacillary, active and inactive during the four surveys.
2. Age and sex-specific rates of prevalence.
3. Trends of incidence of fresh disease during the three successive 2½ years' periods.
4. Fate of inactive disease.

39 Changing Pattern of National TB Association

Shri B.H. Cariappa, India

40. The Role of the Womens' Society Played in Anti-tuberculosis Activities in Japan

Dr. M. Yamaguchi, Japna

It is noteworthy that the response rate of community inhabitants to the mass X-ray examination shows a rising trend with the anti-tuberculosis movement on the part of women's society, thus contributing to the reduction of tuberculosis prevalence within the community concerned. Since the role of the housewives in the anti-tuberculosis campaign has been fully appreciated, JATA has endeavoured to organize "community women's anti-tuberculosis societies" throughout the country, encouraging them to participate in the social action under the slogan: "Stamp out tuberculosis by the hand of woman!"

At present, nearly all prefectures in Japan have several women's anti-tuberculosis societies on local level, and eight prefectures and one major city succeeded in establishing prefectural or municipal unions. In addition, more than a dozen prefectures have women's societies which give priority to anti-tuberculosis campaign, although their scope of action is not restricted within tuberculosis control. The story of historical development of the *Nagano* Prefectural Union, the oldest in Japan, was dramatically introduced in the special issue of "T", the quarterly review of the IUAT, No. 4, December 1962.

The first national meeting of these prefectural societies was held in *Nagano* in 1963 attended by some 1900 delegates and, in July 1965, the first three-day national seminar for some 100 leading members of these societies was held at *Gotemba*. Since then, the "*Gotemba Seminar*" has been held every year growing up to a four-day seminar

attended by hundreds of participants.

They are briefed on the present status of tuberculosis problems and trained on their role in organizing voluntary anti-tuberculosis movements in their communities. They are particularly encouraged to participate in the public relations campaign, contributing to better success of the mass examination, the Double-Barred Cross Seal Sales, etc.

41. Pilot Project in India

Dr. B. K. Shyam Singh, India

The Voluntary Organisation like Tuberculosis Associations have to change their activities, owing to the change their activities, owing to the change in conditions that have arisen as a result of use of Anti-Tubercular drugs in the treatment of tuberculosis. With the advent of Anti-biotics and with the realisation of the responsibility by the Government about the Health Problem of the Nation, where programmes have been implemented detection, treatment and rehabilitation of Tubercular patients by the Governments, expecially in developing and underdeveloped countries, the programmes of the voluntary organisations have to change. This has been very well shown in the Pilot Project study at Tumkur District, by the Mysore State TB Association, a voluntary organisation. The Mysore State TB Association was able to establish a core of volunteers all over the district of Tumkur with a population of 1.5 million in an area of 4073.7 sq. miles having nearly 3000 TB patients spread far and wide in the district, to look after the Tuberculous by the socially minded volunteers who happened to be a relative or neighbour or a friend of the patient without costing much to the Association. The main function of

these volunteers is to supervise the treatment part of the District TB Control Propramme implemented under National Tuberculosis Control Programme. The way in which the volunteers were recruited, trained and implemented, has been given in detail in the text. As a result of this new activity, following inferences have emerged.

(i) Local community got enlightened about tuberculosis problems and hence were responsible for TB Association to be developed in Tumkur District.

(ii) By the Volunteers action, the number of patients becoming defaulters reduced and the revival of defaulters also assured to a great extent.

(iii) Propaganda and spread of Health Education about Tuberculosis permiated through each volunteer reached every nook and corner of Tumkur District in a short time and thus each volunteer become an Health Education Extension Officer.

(iv) Each volunteer now working as an unipurpose worker at present has a chance of becoming multi-purpose worker looking after various other health problems like Leprosy, Family Planning and so on and thus befitting himself as a Basic Health Worker with little more orientation and training.

(v) How co-operation between local community, State TB Association and national and international organisations resulted in the organisation of Projects like Tumkur Pilot Project.

42. Early Tuberculosis Beginning with Neurotic Symptoms

Dr. Yun Kyu Park, Republic of Korea

It is well known that the initial symptoms of pulmonary

tuberculosis are slight fever cough and sputum or hemoptysis, even though we often find asymptomatic patients. On the other hand, it was also reported previously by Pottenger et al that some patients complain of neurotic symptoms at the outset of tuberculosis.

The following patient on whom the author has had experience in the past, may be presented as a possible case of this condition. The patient suffered from insomnia and pain in the shoulder in July '55. Chest X-ray and laboratory tests showed no pathological changes. The patient was diagnosed as neurosis by his attending doctor at that time. A 2nd chest X-ray was taken in november '56 and revealed small densities on both upper lung fields.

In october 1964, Prof. Koga, Jikeikai School of Medicine, Tokyo, Japan, reported tuberculosis beginning with neurotic symptoms, so-called "Camouflaged Tuberculosis" at the International Congress on Diseases of the Chest in Mexico.

Many researches have been made clinically and experimentally at Koga clinic at which the author has worked, to establish the diagnosis of early tuberculosis beginning with neurotic symptoms before showing abnormalities on the chest X-ray or sputum examination. The neurotic symptoms at the beginning of early tuberculosis are explained as an example of General Adaptation Syndrome from the view point of Selye's theory. Selye reported that in the presence of emotional stress or other factors, the adrenal cortex excretes excess corticoid hormones. This phenomenon results in disharmony in the vegetative nerve system and brings various symptoms. Infection from tubercle bacilli may be one factor of stress causing hyperfunction of the adrenal glands.

Modern methods of diagnosis for tuberculosis such as

chest X-ray and sputum examination are not satisfactory to find so-called camouflaged tuberculosis.

The most important method is examination of the eye fundus to find chronic retrobulbar optic neuritis. Many theories have been reported about the cause of optic neuritis. Dr. Saigo, Koga clinic, reported 70% of optic neuritis among 80 patients suspected of so-called camouflaged tuberculosis.

The author obtained satisfactory results recently on the treatment of several optic neuritis patients with anti-tuberculosis drug therapy.

The author also observed optic neuritis by ophthalmoscopic examination and fundus photo on a $2^1/_2$ months old bady who had had BCG vaccination immediately after birth. Tuberculin reaction on the bady showed positive.

43. A Survey of the Knowledge, Attitudes and Practices on Tuberculosis in the Northern Area of Taiwan

Mr. S. T. Wu, Republic of China

1. Motivation

The knowledge, attitudes and practices on tuberculosis of the people in a given area is a fundamental factor in determining the tuberculosis control program in that area. The tuberculosis control program has been operated for more than twenty years in Taiwan. We believe that our people have now a clearer understanding of tuberculosis than ever before, yet we do not know the degree of their understanding, the particular weaknesses of their knowledge, and their attitude toward tuberculosis. We have given to

the people some amount of health education in tuberculosis control over these years, but we are still left in the dark as to whether what we have done really meets the needs of the people, and the effect of such an education. Moreover, we also need to ascertain whether the general public heve a clear understanding of what services our government have rendered in tuberculosis control, whether they are making good use of the services, and what their attitudes toward these programs are.

2. Aims

1. Determining the people's knowledge, attitudes and behaviors on tuberculosis.

2. Determining the degree of confidence the people put on our public tuberculosis control agencies.

3. Determining how much the people understand the free public services in tuberculosis control, their attitude toward such services and how far they are making use of them.

4. Setting a better tuberculosis control program, especially in its educational aspect, based on above data, so that we may be able to offer better services.

3. The Main Points in the Survey

1. The understanding of the causes of tuberculosis.

2. The understanding of the fact that tuberculosis is an infectious disease.

3. The understanding of the fact that tuberculosis in its early stage reveals no symptoms.

4. The understanding of the fact that everybody is susceptible to tuberculosis.

5. The attitude toward the fact that ones self is also susceptible to tuberculosis.

6. The understanding of the methods of tuberculosis examination.

7. The understanding of the use of BCG.

8. Chest X-ray examination in the past and its motivation.

9. The attitude toward free examination by mobile X-ray units

10. The opinion as to where is the best place to go for tuberculosis examination and treatment.

11. The understanding of the most effective treatment of tuberculosis

12 The attitude toward tuberculosis patients.

13. The attitude toward tuberculosis as a disease.

14. The understanding of, and attitude toward, free tuberculosis examination and treatment given by health stations.

4. The Scope, Object, and Date of the Survey

1. The Scope of Survey: It is our final objective that the result of this survey should represent the whole Taiwan Area. Our scope of survey, therefore, will extend to the whole western area of Taiwan, including approximately 12,000,000 inhabitants out of the 13 million odd population in Taiwan. The eastern area and the off-shore islands have to be excluded-regrettably-because of inconvenience in transportation. By means of the random sampling method, we choose at random a total of 19 sampling areas, which represent various degrees of urbanization, 5 from large cities, 2 from small cities, 5 from towns, and 7 from

villages. These sampling areas are distributed over the 14 counties and cities out of the 20 counties and cities in Taiwan. From each sampling area, we then choose 10 *tsun* or *li*; from each *tsun* or *li* we choose 3 *lin*; from each *lin* we choose 6 households; from each household we choose one individual as the object of our interview. Thus, the number of the sampled individuals is 180 in each sampling area, totaling 3,420 samples in the whole Taiwan Area.

We have concluded part of this survey as its first stage, the result of which is submitted herewith to this conference. The scope of survey in this first stage includes 8 sampling areas in northern Taiwan—3 from large cities, 1 from small city, 2 from towns, and 2 from villages—totaling, 1,440 samples.

2. Objects of Survey: Individual of both sexes aged 20-49.

3. Date of Survey: August 10 to September 19, 1970.

5. Methods of Survey and Statistic Analysis

1. Method of Survey: Field interview.

2. Interviewers: Ten interviewers, all of them public health nurses graduated from nursing colleges. The interviewers were given three days of training in interviewing technique before their work.

3. Inspector: Wu Shi-tang, Chief of Training Department, Taiwan Provincial Tuberculosis Control Bureau. He is responsible for checking the results submitted by the interviewers.

4. Statistic Analysis: The data are then processed by the Taiwan Provincial Institute of Family Planning for statistic analysis by the IBM electronic computer.

44. TB Control and Family Planning Programme

Dr. M. L. Mehrotra, India

From January 1966 to December 1969, 54506 index cases who reported by their symptoms or referred by private medical practitioners, from Agra District in which the institution is situated and neighbouring districts, were registered and examined. 35445 contacts of these index cases were also registered in a separate contact clinic and examined.

Of the 54506 index cases examined, 27258 were diagnosed as having pulmonary tuberculosis 10192 were sputum positive and rest 17066 were X-ray positive only. Among the contacts 147 were found sputum positive and 2114 were X-ray positive.

Almost all cases who were diagnosed, put on antitubercular treatment. Sputum and X-ray result of these patients at the end of the treatment will be presented.

As a principle every suitable index cases is routed through the family planning section of the institution before initiation of treatment and every alternate month during the follow-up period of two years. From November 1966 to December 1969, 33877 index patients were motivated to adopt family planning procedures.

From 1966 to 1969 Lippe's loop was accepted by 2519 female patients, 3385 patients accepted other conventional methods like condoms; And since January 1967 to December, 1969, 453 vasectomy operations were done.

Details of procedure, motivation, acceptability, follow-up and complications will be presented during the Regional Conference.

45. Tuberculosis Control and Family Planning

Dr. Y. Rajashekhara, India

The study of risk of infection in a community will help to understand the magnitude of tuberculosis problem existing in a community and helps to take various measures that one can adopt to Control Tuberculosis and to plan for the eventual eradication of the disease. In India, incidence rate calculated by Bogan from different age groups with average of 5.3%.

By this we can now understand the problem of tuberculosis existing in India. The population of India is nearly 532 million and spread over 19 States comprising of 336 districts and 566878 villages. By the infectivity rate we can expect 7-8 millions of TB patients (1.5%) existing of which nearly 2 millions are infectious. According to National Tuberculosis Survey, tuberculosis is rampent in villages to the same extent as it exist in cities and TB is more in men than in women. It is also seen that majority of males and females suffer from TB between the age of 16 to 40. The peak of prevalanace in males rises with age, and in females the peak is the highest at 35 years and then falls. The most youthful and reproductive part of ones life is most vulnerable for tubercular infection. Under the National TB Control Programme, as envisaged by Government of India, provision has been made for permanent diagnostic and domiciliary treatment service with effective anti-TB drugs organised through District TB Centres in collaboration with General Health and Medical Services and with integrated BCG vaccination. As a result of which, every TB patient in whichever nook and corner of a district may be, will get not only free medical care but also Anti-TB drugs sufficient for one year

and facilities for contact examination also provided. Hence there is every chance for all TB patients to get treated under proper supervision so that TB is successfully treated and spread of infection prevented. More number of TB people now have a chance to live long unlike during pre-drug period when majority would have died.

The population problem in India is much more serious and the population is increasing at the rate of 30,000/— per every hour in India. It has become very difficult for the country to feed the ever increasing population and to give the clothing, housing education and employment would be a tremendous task for Indian Government. Rightly Government of India is trying to fight this population explosion problem on a "Zwar path". Under this programme the marriage age is being increased among males to 24 years and females to 22 years by legilation and is advocating family spacing among younger couples and advocating permanent measures for vulnerable group to go for sterilisation especially if people were to have more than three children both for females and males. Various temporary means like use of condomes, jelleys pills, loops and so on are also being advocated. By these methods, Govt. has been able to check the over growing population problem to a great extent. Various propoganda means have been used to familiarise the idea of small family and its benefit on the society and community and all these have contributed to a great extent in bringing the expected dividend.

With the use of Anti-TB drugs, it has been said that mortality rate and infectivity rates have been brought down to a great extent. Now more number of TB patients have been made to live long, they would centainly help in creating over population problem. In pre-chemotherapeutic periods most of the sterility amongst females used to be due to tuberculosis infection of the genitial tract but now

with the use of Anti-TB drugs these people have given birth to childredn.

As such it is highly desirable to advise the TB patients that while undergoing treatment that they should not indulge in sexual act which would hamper the arrest of the disease, with least chance of another partner getting infection and also not to have children for nearly 3-4 years after the arrest of the disease, if the patient were to be a female, because every act of child bearing will give rise to psychological stress and strain of child bearing and rearing and also physical exertion of child bearing might flare up the disease. If the parties were to have one or two children before the attack of the disease, it is better to advise the parties to adop measures not to have any more children and thereby less chances for relapse due to child bearing can occur. It is also better to impress on patients, the advantages of having a small family thereby more attention could be given to the deceased person and to bring up the existing children in a better atmosphere of socio-economic surroundings. Here, there is more need to stress family planning among TB patients and therefore family planning must form an integral part of TB Control programme.

In Sanatoria, at the time of discharge, patients are given some ideas about family spacing and Family control measures. They are also provided with materials free of cost for practice, of family planning and are advised to contact the nearest family planning centre nearer their homes for any help needed in future. These patients are given, the benefit of social workers when needed, regarding family planning. In the clinics, the social worker provided, will advise and motivate the patients attending the clinic either for clinical investigation or for collection of drugs on family planning and socio-economical benefits

and thus prepares them for family planning. Here also TB patients are provided with materials for the practice of family planning, free of cost. All these have borne results. The births amongst these TB patients have decreased through number of statistical figures could be given.

46. Decade of 70's, Will it Witness the Global Control of Tuberculosis?

Mr. E. J. O'Brien, Canada

47. The Surgical Treatment of Pulmonary Tuberculosis in Taiwan (1951-1969)

Dr. P. Y. Wang, Republic of China

The total number of patients who have received surgical treatment for pulmonary tuberculosis in Taiwan from 1951-1969 is 2,071. Among these patients, 1594 (73.1%) resections have been done. 333 (16.08%) patients have received collapse therapy. 144 (6.95%) patients have been treated with various other kinds of operations.

Among the 2,071 cases, 859 (41.48%) patients lost follow-up post-operatively. The complete post-operative information oblained is from 1,212 (58.52%) cases (Table 1)

Table 1. Results of surgical treatment in 1,212 cases of Thoracic Tuberculosis, 1951-69

Operation	No. of Pts.	Complications	Mortality	Sputum conversion rate
Pneumonectomy	151	26(17.22%)	10(6.62%)	81.57%
Lobectomy	547	64(11.69%)	15(2.74%)	82.30%
Seg. resection	201	18(8.96%)	1(0.5 %)	75.60%
Local resection	23	0	0	50.00%
Thoracoplasty	163	8(4.91%)	4(2.45%)	57.93%
Extrapleural plombage	64	4(6.24%)	2(3.12%)	52.90%
Others	63	5(7.49%)	4(6.35%)	56.50%

The operative mortality among these 1,212 patients is 2.97%. The incidence of complication is 10.31%.

Field Trip to Sun-Moon Lake

November 20, Friday, 1970

a.m.	7:30	Bus leaving Ambassador Hotel
	7:45	Arriving Taipei Railway Station
	8:00	Leaving for Taichung City by train
	10:55	Arriving Taichung City
	11:00-12:00	Refreshment at Taichung Restaurant
p.m.	12:10	Leaving for Exhibition Hall
	12:50	Arriving Exhibition Hall
	2:00	Leaving for Sun Moon Lake
	3:30	Arriving Sun Moon Lake
	6:00	Dinner at Ever-Green Hotel
	7:30-9:00	Visit Aborigine Village and enjoy the Aboriginal dancing

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